"CLINICOPATHOLOGICAL STUDY ON MULTINODULAR GOITRE"

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CERTIFICATE

This is to certify that the dissertation titled "CLINICOPATHOLOGICAL STUDY ON MULTINODULAR GOITRE" is the original work done by DR.N.ARUNMOZHI VIJAY , post graduate in the department of GENERAL SURGERY, TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI-11 submitted to THE TAMIL NADU DR.MGR MEDICAL UNIVERSITY, Chennai – 32 towards the partial fulfillment of the requirements for the award of M.S degree in GENERAL SURGERY April 2014 examination.

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CONTENTS

ABSTRACT

CLINICOPATHOLOGICAL STUDY ON
MULTINODULAR GOITRE

INTRODUCTION

MULTINODULAR GOITER describes an enlarged, diffusely heterogeneous thyroid gland.Initial presentation may include diffuse enlargement, but the mass often develops asymmetrical nodularity. The cause of this mass is usually iodine deficiency. Initially, the mass is euthyroid; however, with increasing size, elevations in T3 and T4 can occur and progress gradually into clinical hyperthyroidism.

Work-up and diagnosis include evaluation of thyroid function tests. Ultrasound and radioisotopic scanning demonstrate heterogeneous thyroid substance. Nodules with poor uptake can present as lesions suspicious for malignancy.The incidence of carcinoma in multinodular goiter has been reported as 5% to 10%. Therefore, FNAC for diagnosis and resection for suspicious lesions should be considered.

Hyperthyroidism may be adequately controlled by drugs, but surgical management is the preferred treatment. Subtotal or total thyroidectomy may performed depending upon the involvement of the thyroid gland. Radioactive iodine therapy is reserved for elderly individuals who represent poor operative risk.

The complications of thyroid surgeries are heamorrhage, respiratory obstruction, vocal cord paralysis, hypoparathyroidism, thyroid insufficiency, thyrotoxic storm and wound infection.

KEY WORDS : Multinodular Goitre, Presenting Complaints, Fine Needle Aspiration Cytology, Thyroidectomy,

MATERIALS AND METHODS

This is a prospective clinical study of randomly selected patients admitted in the department of surgery, TVMCH diagnosed and treated as a case of multinodular goitre during the study period.

The patients diagnosed as a case of multinodular goitre will undergo detailed history taking, clinical examination, investigations like CBC, thyroid profile, fine needle aspiration cytology, x – ray chest and neck and ultrasonography of neck. After surgery, the patients will be followed up for any immediate post operative complications. The specimen will be sent for histopathological examination and the results will be recorded.

Through this study I intend to find out

Through this study I intend to emphasize the existing data regarding multinodular goitre and find out

- Whether there is a specific age distribution for multinodular goitre in and around tirunelveli.
- To study and discuss the most common presenting clinical features of multinodular goitre.
- The percentage of thyroid malignancies presenting as multinodular goitre and whether FNAC is conclusive in confirming the diagnosis, which will be helpful in planning the surgery necessary ie., whether a subtotal or total thyroidectomy must be performed.
- The percentage of post operative complications encountered in surgeries performed for multinodular goitre in our hospital.

RESULTS

In our study, among the 50 cases three were male which constitutes 6% of the study group. The remaining 47 cases were females (94%). Majority of the cases were in the 30 – 40 years age group (32%), followed by the age group of 40 – 50. The Mean age of incidence was 42.26. The average post operative stay among the 50 cases studied was 5.3 days. 76% of the cases were discharged between 4 to 6 days of post operative stay. The presenting complaint was a swelling in all the cases studied (100%). The swelling was associated with pain in 48% of the cases. Pressure symptoms like dysphagia, dyspnoea and hoarseness of voice were present in 44%, 18% and 20% of cases respectively with an average of 27.3%.Of the 50 cases of Multinodular goiters studied, 7 cases were hyperthyroid on presentation which constitutes 14% of the cases. All the cases were taken up for surgery, 88% of cases underwent total thyroidectomy and 10% of cases underwent subtotal thyroidectomy. The Fine Needle Aspiration Cytology reports of the 50 cases showed Nodular Colloid Goitre (64%) as the most common FNAC finding followed by Hashimoto's Thyroiditis (11%). The FNAC report was follicular neoplasm for 2 cases, so total thyroidectomy was performed in those cases to rule out malignancy. Post operative complication occurred in three cases. The post operative histopathological examination of the resected specimen showed that 37% of the cases were Colloid nodular goitre and 18% of cases had features suggestive of Hashimoto's thyroidits. One case of papillary and follicular carcinoma each.

CONCLUSION

MULTINODULAR GOITRE is more common among females and in the age group of 30 to 40 years and is more common among females. The chief complaint in most of the patients is swelling in front of the neck and is associated with pain in 48% of the cases. The average post operative stay in the hospital was

5.3 days. Post operative stay in hospital has to be reduced. Thyroidectomy can be done as a day care or short stay procedure in our hospital as is the recent trend in developed countries. However, the applicability of these practices to thyroid surgery remains controversial. Day care surgery can be promoted in selected and educated patients as this will be the future of thyroid surgeries. Hyperthyroidism in multinodular goitre was present in 14% of cases. Hyperthyroidism occurs in cases of multinodular goitre in the natural evolution of the disease and the patient must be treated and brought to euthyroid state before surgery.

Fine Needle Aspiration Cytology is a very useful investigation in the evaluation of Multinodular goitre except for that it cannot differentiate follicular adenoma from follicular carcinoma. Most of the cases had colloid nodular goitre in multinolar goitre. Carcinoma in not uncommon in cases of Multinodular goitre. So, suspicion should always be present. Total thyroidectomy is the preferred surgery for multinodular goitre. But subtotal thyroidectomy may also be performed in cases in whom surgery is done for cosmetic reasons as in Hashimoto's thyroiditis. Hemithyroidectomy can be an option in Multinodular goitre if the nodules are confined to one lobe and the patient is aware of the possibility of recurrence and is willing for regular follow up. Post operative complications after thyroidectomies for multinodulargoitre are less in our institution as compared to various studies. Visualization of the recurrent laryngeal nerve during surgery is an important factor contribution to the low incidence of nerve injuries in our study group.

INTRODUCTION

Multinodular goiter describes an enlarged, diffusely heterogeneous thyroid gland. Initial presentation may include diffuse enlargement, but the mass often develops asymmetrical nodularity. The cause of this mass is usually iodine deficiency. Initially, the mass is euthyroid; however, with increasing size, elevations in T3 and T4 can occur and progress gradually into clinical hyperthyroidism.

Work-up and diagnosis include evaluation of thyroid function tests. Ultrasound and radioisotopic scanning demonstrate heterogeneous thyroid substance. Nodules with poor uptake can present as lesions suspicious for malignancy.

The incidence of carcinoma in multinodular goiter has been reported as 5% to 10%.Therefore, FNAC for diagnosis and resection for suspicious lesions should be considered. Hyperthyroidism may be adequately controlled by drugs, but surgical management is the preferred treatment. Subtotal or total thyroidectomy may performed depending upon the involvement of the thyroid gland. Radioactive iodine therapy is reserved for elderly individuals who represent poor operative risk.

The complications of thyroid surgeries are heamorrhage, respiratory obstruction, vocal cord paralysis, hypoparathyroidism, thyroid insufficiency, thyrotoxic storm and wound infection.

AIMS AND OBJECTIVES

AIM OF THE STUDY

- To study the age and sex distribution of multinodular goitre
- To study the presenting clinical features in multinodular goitre
- To study the correlation between FNAC and histopathological examination
- To study the incidence of malignancy in multinodular goitre
- Discuss the various treatment modalities available in our hospital
- To study the incidence of various post-operative complications

INCLUSION CRITERIA

- All cases admitted in the department of surgery diagnosed as a case of multinodular goitre
- Above the age of 20 yrs
- Cases presenting with both toxic and non toxic features

EXCLUSION CRITERIA

- Age less than 20 yrs
- Pregnant women
- Cases presenting with solitary nodule
- Cases with diffuse enlargement of thyroid gland

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Through this study I intend to emphasize the existing data regarding multinodular goitre and find out

- Whether there is a specific age distribution for multinodular goitre in and around tirunelveli.
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REVIEW OF LITERATURE

- The name “THYROID” is derived from the Greek word for “shield-shaped gland in the anterior part of the neck” (Thyroides).
- Thyroid gland was referred to as “laryngeal gland” and subsequently named as “THYROID” by Wharton in 1645.
- The relationship between endemic goitre and Cretinism was showed by Paracelsus (1492-1591).
- In 1874, Gull described Cretinoid changes in adults.
- Curling in 1950 accounted of Cretinism at London and recorded complete absence of thyroid gland in both cases.
- Thyroxine was isolated by Kendall (1965). Harrington and Banger in 1927 synthesized thyroxine. Triiodothyronine was discovered by Cross, Pittrivers and Roche in 1953. Radioactive iodine was introduced in 1934 which made clear the understanding of the physiology of thyroid gland.

SURGERY IN THYROID

Roger Frugardi of Salerno in Bamberg manuscripts gave the first credible account of thyroid gland in 1170.

The first well-documented partial thyroidectomy was performed in Paris in 1791 by Pierre Joseph Desault. Guillaume Dupuytren performed total thyroidectomy in 1808 for a goitre weighing 1.2kg. In 1821, Johann Hedenus

successfully removed six “suffocating goitre” by ligation of all the arteries and dissection. Most of the thyroid surgeries were disastrous up to the second half of the 19th century due to bleeding and sepsis.

Following the advent of general anaesthesia (1890), antisepsis (1860’s) and haemostasis (1870’s), surgeons were able to do more thyroid operations and improvise techniques with great reduction in mortality.

The collar incision was introduced by Tules Boeckial (1848-1927) of Strasbourg. The first transplantation of thyroid gland was done by Pays in 1906.

In the late 19th century, two surgeon-physiologists Theodor Billroth and Emil Theodor Kocher revolutionized the understanding and management of thyroid diseases. They established large clinics in Europe and developed skilled techniques of surgery, provided surgical results that proved the safety and efficacy of thyroidectomies for both benign and malignant diseases. Kocher received the Nobel Prize in 1909 for his pioneering developments in the understanding of thyroid physiology.

The 20th century began with the contribution of Billroth and Kocher. All the advances have allowed the diagnosis and treatment of thyroid diseases to become rapid, cost-effective and low morbidity procedures.

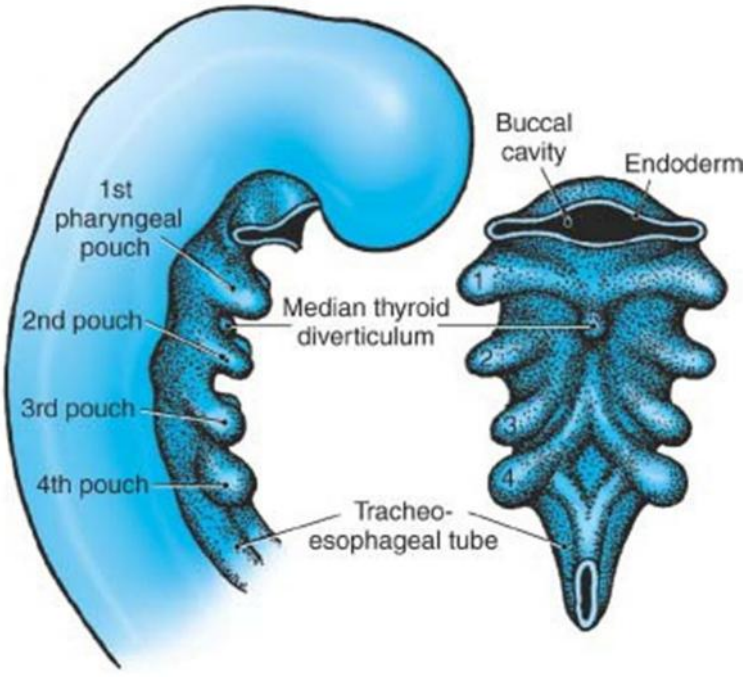
EMBRYOLOGY

The tissue bud that becomes the thyroid gland arises as a median diverticulum in the floor of the “primitive pharynx”, caudal to the

tuberculumimpar. It originates from the primitive alimentary tract, which are cells of endodermal origin. This cellular structure descends into the neck region to develop into a bilobed solid organ.

The original attachment in the pharynx is at the foraman caecum through the thyroglossal duct which reabsorbs after 6 weeks of age. The distal end of this remnant matures as a pyramidal lobe.

Thyroid follicles first appear as the lateral lobes of thyroid gland develop. Follicles begin to synthesis colloid when the embryo is 6cm in length. In the 3rd month, iodine trapping and thyroid hormone secretion begins.

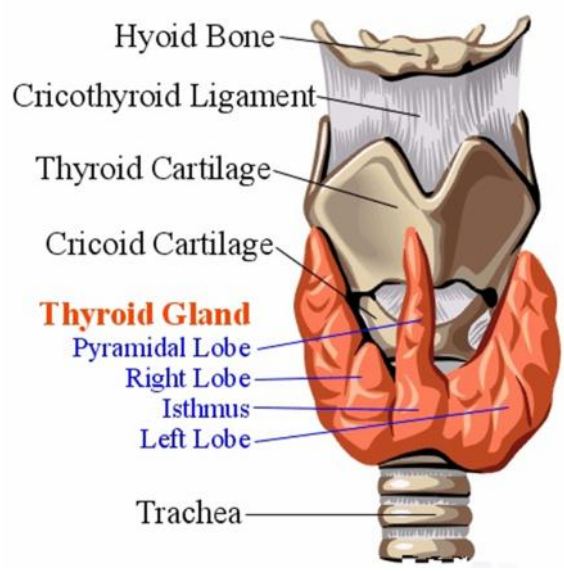


SURGICAL ANATOMY OF THE THYROID GLAND

Normally adult thyroid gland weighs 20 – 25 gms. It is a bilobed structure connected by the isthmus that lies in front of the thyroid cartilage. The thyroid

gland encircles about 75% of the junction of the larynx and the upper part of the trachea. The gland lies against C5, C6, C7 and T1 vertebrae. The isthmus covers the 2nd to 4th tracheal rings. The pyramidal lobe is found in about 30% of patients.

The thyroid gland is surrounded by a thin layer of connective tissue which is called the true capsule. The false capsule is derived from the pretracheal layer of the deep cervical fascia. These capsules are pierced by blood vessels of the thyroid gland to form a plexus beneath the true capsule. So the thyroid gland is removed with its true capsule. The thickening of fascia that fixes the back of each lobe to cricoid cartilage is called the Ligaments Of Berry.



Relations

- Superficial surface is covered by
    - Sternohyoid
    - Superior belly of omohyoid

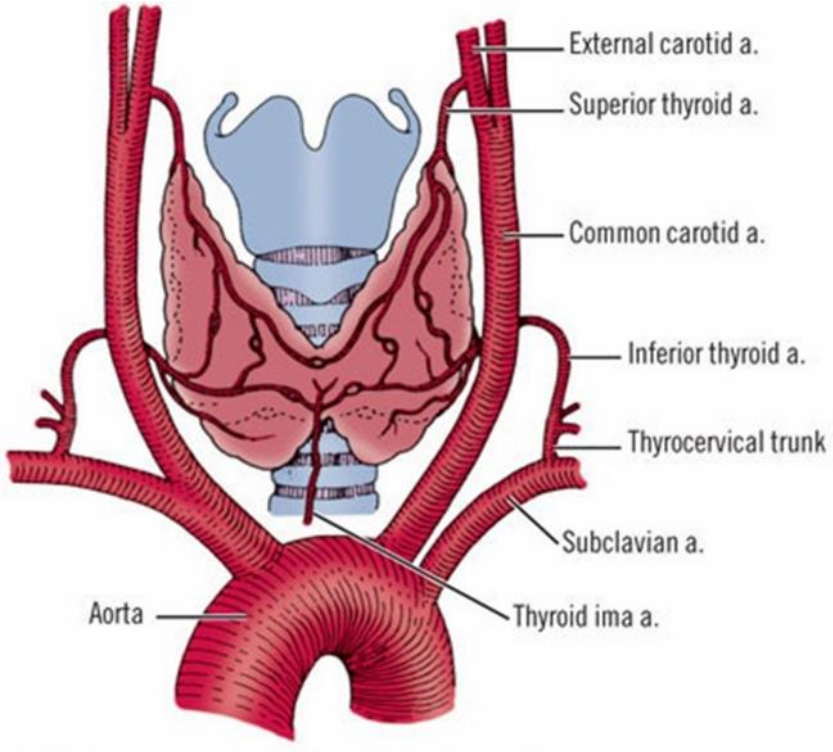
    - Sternothyroid
    - Anterior border of sternocleidomastoid
- Medial surface is related to
    - Trachea and oesophagus
    - Inferior constrictor and cricothyroid
    - External laryngeal and recurrent laryngeal nerves
- Posterior surface is related to the carotid sheath
- Anterior border is related to the anterior branch of the superior thyroid artery
- Posterior border is related to
    - Inferior thyroid artery
    - Thoracic duct on the left side
    - Parathyroid glands

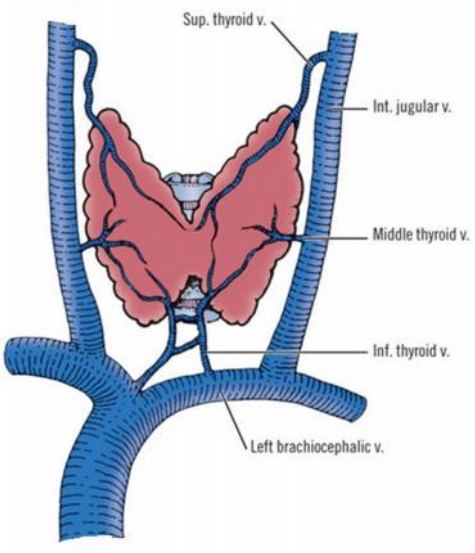
Blood supply

Arterial supply consists of four main arteries, two superior and two inferior thyroid arteries. Superior thyroid artery is the first branch of the external carotid artery and arises just above the bifurcation of the common carotid artery. The inferior thyroid artery takes origin from the thyrocervical trunk.

The thyroid gland is drained by three pairs of veins. The superior thyroid vein lies immediately adjacent to the superior arteries and drains into the internal jugular vein. Middle thyroid vein is present in about 50% of patients. It

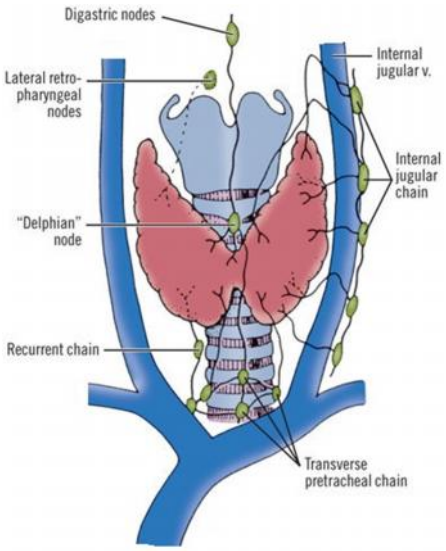
is short and lies horizontally. Usually there are two or three inferior thyroid veins draining into the innominate and brachiocephalic veins.





Lymphatic drainage

The thyroid gland has rich lymphatics draining it in almost every direction. The lympyhatics are present immediately beneath the capsule and communicates between the two lobes through the isthmus. They drain into the regional lymph nodes occupying the pretracheal, paratracheal and trachea-oesophageal lymph nodes.



Nerve supply

Sympathetic nerve supply is mainly derived from the middle cervical ganglion and partly from superior and inferior cervical ganglion. They are vasoconstrictors.

Nerves related to the thyroid gland

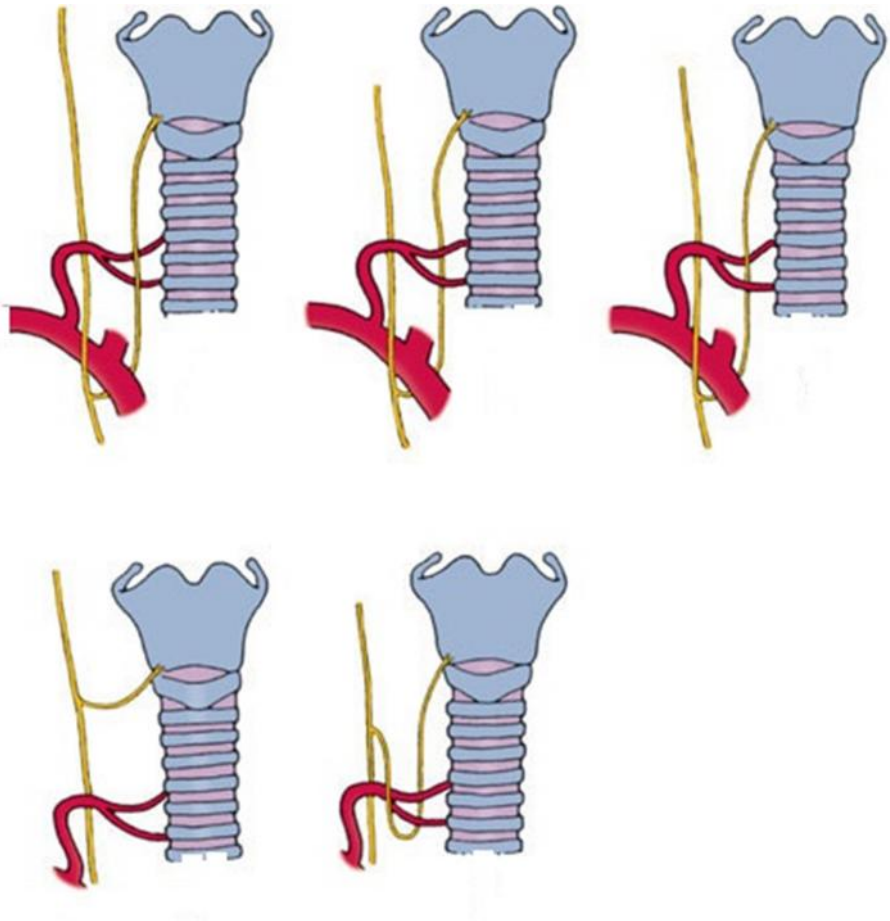
Right Recurrent laryngeal nerve :

It branches from the vagus→ loops around the subclavian artery → crosses behind rt. Common carotid → in or near tracheoesophageal groove → post to rt. Lobe of thyroid → enters the larynx

Left Recurrent laryngeal nerve :

Arises where the vagus crosses the aortic arch → loops under ligamentum arteriosum→ ascend like the rt. Nerve. Both nerves cross the inf. Thyroid artery near the lower border of middle third of the gland

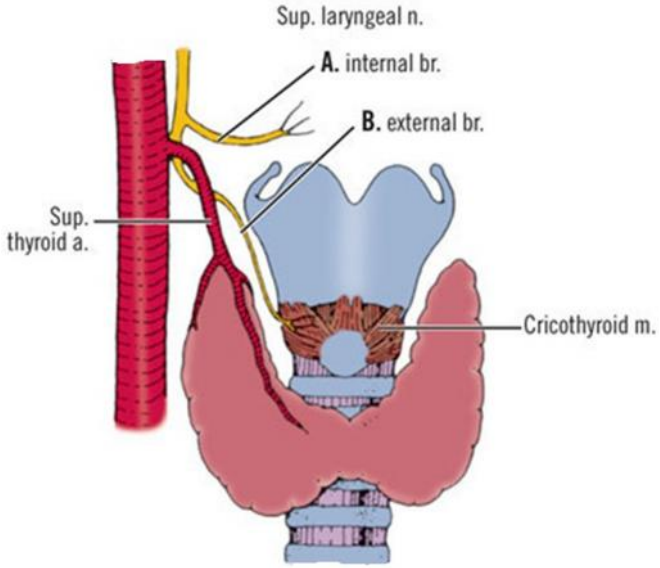
The nerve can be identified posterior to the inf. Cornu of thyroid cartilage where it enters the larynx. Lower down, the nerve can be palpated as a tight strand over the trachea



External laryngeal nerve :

Branch of superior laryngeal nerve. Arises at the level of superior cornu of hyoid bone. Supplies cricothyroid and cricopharyngeus muscles.The nerve

passes under the sternothyroid along with the superior thyroid vessels, Medial to them.



PHYSIOLOGY OF THE THYROID GLAND

Thyroid gland is responsible for the production of two families of metabolic hormones

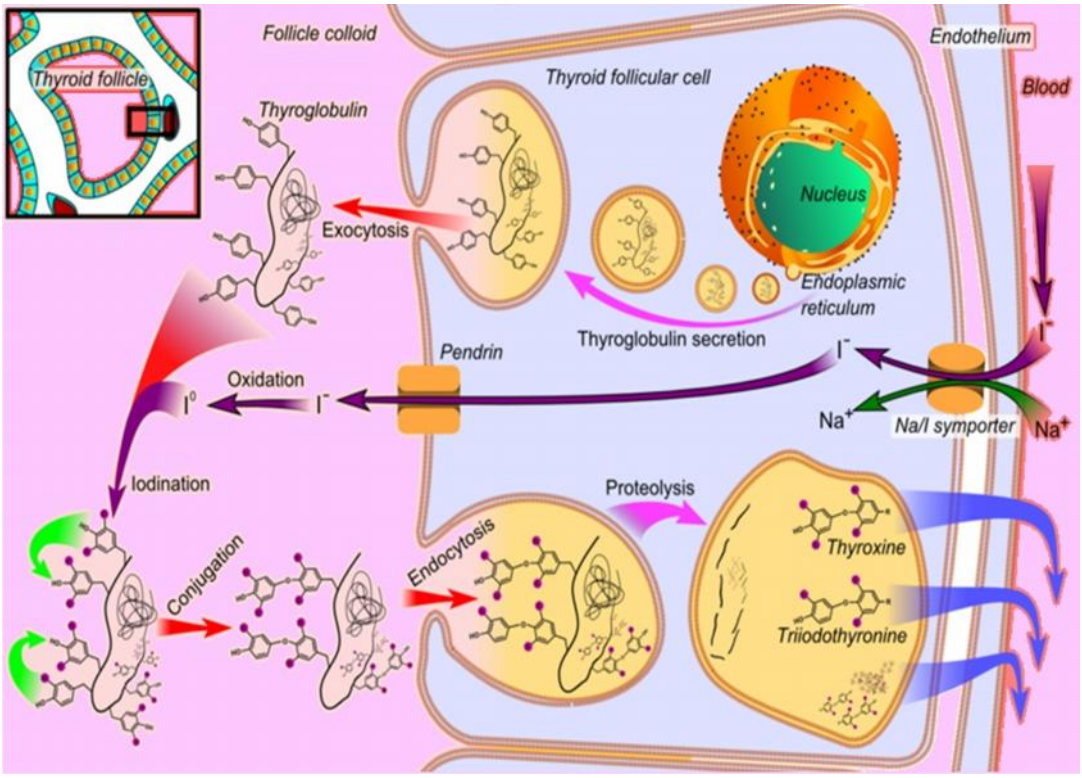
- Thyroxin (T4) and Tri-iodothyronine (T3)
- Calcitonin – the hormone regulating calcium

Iodine metabolism

Iodine is essential for the production of thyroid hormones. It is absorbed from the gastrointestinal tract in the form of inorganic iodide and enters the extracellular pool. The thyroid gland is responsible for storing 90% of the total

body iodine. It is stored in the thyroid as preformed hormone or as an iodinated amino acid.

Iodine is transported into the follicular cells via an intrinsic transmembrane protein located in the basolateral membrane. Inside the follicle, it is rapidly oxidized and bound to thyroglobulin.



Thyroid hormone synthesis

Once organic iodide is oxidized and bound, it couples to thyroglobulin with tyrosine moieties to form iodotyrosinesmonoiodotyrosine and diiodotyrosine. It is dependent on thyroid peroxidise, an important intracellular catalytic agent.

Coupling of monoiodotyrosine and diiodotyrosine which are biologically inert gives rise to the active thyroid hormones T4 and T3. Under normal

circumstances, T4 formation predominates. Both T3 and T4 are bound to thyroglobulin and stored in the colloid in the centre of the follicular unit, which allows quicker secretion of the hormones. Most of the thyroid hormones released from the gland is T4, which is deiodinated in the peripheral tissues and is converted to T3.

The apical membrane of the follicular cells regulates the release of T3 and T4 via lysosymal hydrolysis of the colloid containing the thyroglobular bound hormones.

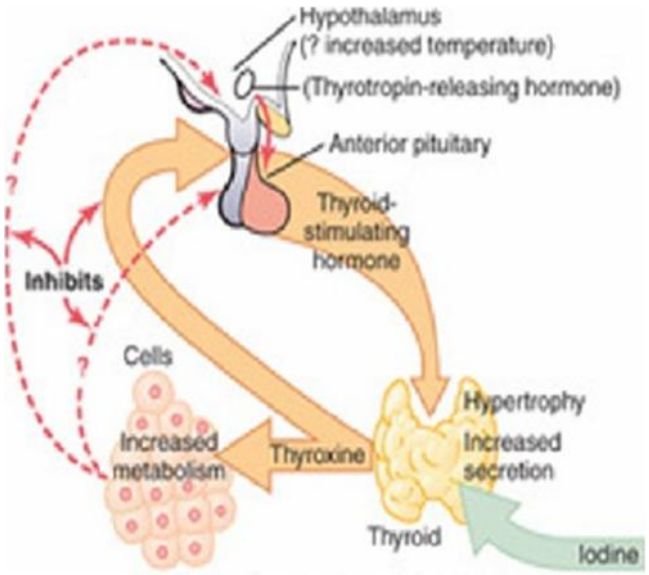
On entering the circulation, the hormones are largely bound to a protein called thyroxine-binding globulin. The protein has more affinity to T4 than to T3. The free hormone is physiologically active and the protein-bound fraction acts as a reserve.

REGULATION OF THYROID HORMONE SYNTHESIS

The hormone secretion from the thyroid is controlled by anterior pituitary by Thyrotropin (TSH). Thyrotropin is a 210-amino acid, two-chain glycoprotein. It induces hyperplasia and hypertrophy of the thyroid follicles and increases blood supply to the gland, promotes trapping of iodine and organification of iodine.

Synthesis and release of TSH is controlled by the hypothalamus through the thyroid-regulating hormone. The negative feedback inhibition to TSH

secretion is provided by the thyroid hormones. Tri-iodothyronine has been shown to reduce TRH receptors on thyrotropes.



ACTIONS

I. Growth and development

T3 and T4 are essential for normal growth and development. Congenital deficiency resulting in cretinism emphasizes their importance. The developmental milestones are delayed and practically all the tissues are organs in the body suffer. The nervous system is the greatest sufferer. Adult hypothyroidism also results in impairment of intelligence and the movements become slow.

II. Intermediary metabolism

a. Carbohydrate

There is increased utilization of carbohydrates, glycogenolysis and gluconeogenesis in liver along with faster absorption of

glucose from intestines. There is hyperglycemia, and diabetes-like state with resistance to insulin occurs in hyperthyroidism.

b. Lipid

Thyroid hormones indirectly enhance lipolysis by potentiating the action of catecholamines and other lipolytic hormones. The plasma free fatty acid levels are elevated. Lipogenesis is also stimulated. Hyperthyroidism is characterized by hypercholesterolemia. Low-density lipoprotein levels are reduced in blood.

c. Protein

The overall effect of T3 is catabolic. Increased amount of protein is being used as energy source. There is negative nitrogen balance and tissue wasting. Weight loss is a feature of hyperthyroidism.

III. Calorigenesis

Thyroid hormones increase basal metabolic rate by the stimulation of celluar metabolism and resetting the energystat.

IV. Cardiovascular system

T3 and T4 cause a hyperdynamic state of circulation. This is secondary to increase in peripheral demand and partly due to direct

cardiac action. Heart rate, cardiac output and contractility are increased. Atrial fibrillation and other irregularities are common in hyperthyroidism due to the direct action of T3 and T4 by direct action on contractile elements.

V. Nervous system

Thyroid hormones have profound functional effect on the CNS. Mental retardation is the hallmark of cretinism. Hyperthyroid individuals are nervous, excitable, anxious and exhibit tremors.

EPIDEMIOLOGY

Multinodulargoitre is world-wide in distribution. It is prevalent among all races, in all climates and at all altitudes inhabited. It occurs both sporadically and endemically. Most of the endemic areas are mountainous (Sapaus, 1960).

In India, about 71 million people suffer from iodine-deficiency disorder and another 200 million people are at risk. A national survey conducted by the Indian Council of Medical Research (ICMR) in 1989 showed goitre prevalence of 6.9% (in all age groups). There is a total goitre rate of about 13.5% in children. In Tirunelveli district, the prevalence is about 7.0% which is less compared to the Nilgiris where it is 16.6%.

The Goitre Subcommittee of Medical Research Council of Great Britain concluded that the mechanism of goitre is due to the failure of thyroid gland to obtain iodine sufficient to maintain normal function and structure. The failure is usually due to an absolute environmental iodine deficiency. It may also be caused by factors interfering with dietary iodine availability, which in turn imposes an abnormal demand on the thyroid gland.

ETIOLOGY

Marrine a trained pathologist did studies on goitre. One of the classical experiments in public health shows iodine as a prophylactic supplement. The recent introduction of tracer methods, urinary radioactive iodine and technique of chromatography has provided new opportunities for an understanding the etiology and pathogenesis of nodular goitre. He demonstrated an inverse relationship between iodine contents of the gland and degree of epithelial hyperplasia. Vanfallen berg and Mac lendon showed an inverse relationship between the level of iodine present in food and drinking with the incidence of goitres.

The most recent phase of study is with the use of radioactive iodine. The pioneering study by Stanburg in Argentina and followed by similar studies in India, Holland, Finland and Congo have yielded results are consistent with iodine deficiency hypothesis.

Goitrogens

There is evidence that Thiocynates and Thiouracil like substances exist in food habitually consumed by man. Thiocynates inhibit the ability to concentrate iodine and thyroid hormones synthesis. Clement was of opinion that plant goitrogens are unlikely to be significant etiological factors in thyroid diseases.

Factors other than iodine deficiency

There are two well-documented epidemics in which the observed features do not fit with the iodine deficiency hypothesis. Clement observed that school children in Southern Tasmania developed seasonal goitre even though they have intake of large iodine supplement. This seasonal increase in goitre incidence appears to coincide with the spring flush of postures and weeds. Strong evidence was presented to suggest that a goitrogen in milk from the cows fed on such postures caused thyroid enlargement. Boys and girls are equally affected unlike in epidemics where girls predominate.

Coster of Italy showed another exception to iodine deficiency hypothesis. He observed in several epidemics that iodine levels may be normal or elevated, PBI were within the normal range and water and urinary iodine values, were not different from non endemic region. Coster stated that there were some strong ties between endemic and epidemic goitres in these regions.

Calcium and Fluorine

The association of lime stone formation with endemic goitre in hard water was observed by many over the years leading to hypothesis that excessive ingestion of calcium may be an aetiological factor. Some experimental evidence have indicate that calcium may enhance the goitrogenic effect on the diet which is already deficient in iodine. Wilson suggested that excessive fluorine in also a causative factor.

Thyroid nodule following therapy with I131

Younger the patients, greater is the chance of thyroid nodules developing following radioiodine therapy for thyrotoxicosis. Nodules usually originate from focal hyperplastic and regenerated areas of lobules which is apparently due to prolonged TSH stimulation on the tissues which are still able to react.

Familial Goitres

Defect in organification failure to form organic iodine

Defect in iodine transport

Deficiency of enzymes

Lack of Iodine Peroxidase – complete block

Lack of Iodine Transferase – incomplete block

Coupling defect – Failure to couple iodo-tyrosines

Abnormal serum iodinated polypeptides

Iodotyrosinedeiodinase defect

Childhood Goitre

The presence of nodules in the thyroid gland in children raises the strong possibility of malignancy. Possibility of malignancy increases when the nodule is single, hard and fails to concentrate radioiodine (cold nodule).

Studies performed at Mayo clinic from 1908 to 1955 showed that, of 130 children with nodular enlargement of thyroid, 68 had adenoma of thyroid, 46 had carcinoma, 5 had goitrous cretinism, 8 had lymphocytic thyroiditis and 3 had congenital goitre. Thus carcinoma accounted for 35.4% of patients with nodular enlargement of thyroid gland. The nature of the diseases producing nodular enlargement in a child can be determined mostly only by histology.

CLASSIFICATION OF THYROID NODULES

There is no universally accepted classification for thyroid nodules, as the etiology of the nodular goitre is presumptuous and correlation of pathological and clinical features is difficult. Any classification must be usable to clinician and pathologist, simple to avoid confusion and workable, so admittable to changes and revisions have been made by the newer concepts.

WHO Classification

Stage	Clinical findings
A	Nogoitre
B	Goitre detectable only by palpation and not visible even when the neck in full extended
1	Goitre palpable, but visible only when the neck is fully extended
2	Goitre visible with the neck in normal position
3	Very large goitre which cannot be recognized at a considerable distance

CLASSIFICATION OF TYPES OF GOITRE IN INFANCY AND CHILDHOOD

I Thyroid enlargement resulting from compensating action of impaired hormonopoiesis.

1.Familial iodine induced goitre secondary to metabolic inborn errors.

- Iodine transport defect
- Organification defect

Lack of iodine transferase

Lack of iodine peroxidase

- Coupling defect

  Iodothyrosinedeiodinase defect.

- Abnormal iodinated polypeptides

2.Endemicgoitre resulting from iodine deficiency.

3.Goitre due to drugs or naturally occurring goitrogens

- Inhibitors of hormone synthesis – Thiourea, Thiouracil, Propyl thiouracil, Methyl xanthine, Methymazole, Sulphonamides, Phenyl butazone and Para aminosalicylates

- Inhibitors of iodine accumulation – Perchlorates, Thiocynates, Nitrates

- Natural goitrogens – Cabbages, Turnips, Soyabeans

- others – Cobalt, Resorcinal, Dihyroquinine

II. Thyrotoxicgoitre

- Neonatal

- Childhood

III. Goitre in Thyroiditis

- Acute

- Subacute (Dequervains)

•Chronic thyroiditis

•Riedel’s thyroiditis

IV. Nodular goitre

•Cysts

•Benign and malignant neoplasms

CLASSIFICATION OF NODULES BASED ON SCINTI SCAN (Warren’s classification):

•Hot nodules – hyper functioning

•Warm nodules – Functioning

•Cool nodules – Hypo functioning

•Cold nodules – Non functioning

PATHOGENESIS OF THYROID NODULES

Thyroid nodules whether simple, toxic or malignant seem to occur as a result of thyroid follicles to lose their dependence on thyroid stimulating hormone - breakdown in the serve mechanism (Selwyn Taylor,1969). Selwyn Taylor suggested that nodules in the nontoxic goitre are initially small foci of

hyperthyroidism. He traced the origin of thyroid nodules back to the stage of simple hyperplasia of follicular cells. At this stage that the goitre is preventable.

Auto radiographic studies

In this method of study, a slice of the thyroid gland exposed to a photographic film, which turns black when the tissue contains radioactive material. Thus it makes possible for compare areas of thyroid gland with its capacity to concentrate and bind iodine to protein, in other words, ability to synthesize thyroid hormones. By this study the evolution of the multinodular goitre is divided into five stages (Selwyn Taylor Hypothesis).

Stage I: Diffuse enlargement of thyroid gland, which shows increase in vascularity.there is a large uptake of radioiodine and with uniform blackening of the auto radiograph. This is typical in puberty goitre but may persist for years.

Stage 2: Discrete areas of focal hyperplasia. There are few patients in whom all functioning thyroid tissue concentrated in a single area. Rawson described this as a toxic nodule in a nontoxic gland. Patient presents with in a euthyroid state.

Stage 3: increased hyperplasia and vascularity of nodules. This stage is charecterised by disruption and haemorrhage. The blood supply in the nodules is by thin walled tortuous dilated vessels, which easily bleed resulting in haemorrhagic necrosis due to compression of surrounding tissue, fibrous pseudo capsule is formed around the nodule with obliteration of small vessel

and formation of Arterio - venous shunt. These perinodular shunts also result in fall in blood supply of the nodule.

Stage 4: Nodules undergo resolution in two ways. Either a large, lace of colloid fills the nodule and this is found to be free of iodine or a mass of new follicles grow to supercede the nodules and their colloid do not take up radioiodine.

Stage 5: The Multinodular goitre is formed by continued repetition of the

above described processes resulting in most of nodules becoming inactive and incapable to metabolize iodine but among them are few active foci, which supply normal body requirement.

In Selwyn Taylor hypothesis, the inference that 'functioning nodule was a stage in the evolution of all nodular goitre' is questioned by Scinti-scan studies to determine the importance of solitary or dominant thyroid nodule. It has been demonstrated that micro or macro nodules occur in the same thyroid gland suggesting that small nodules function in this manner from their origin. Auto radiographic studies have shown that gross autonomous functioning nodules have similar functioning micronodules.

Transition from functioning to non-functioning nodules may occur through degenerative changes or possibly by the simple loss of functional capacity of the follicles. Autonomous micronodules in the gland from the very early stage of disease suggest partial loss of trophic control. The finding of

functioning micronodule with similar macro nodules strongly suggests that the large nodules were functioning throughout the period of growth.

HISTOPATHOLOGY OF MULTINODULAR GOITRE

The initial stage of multinodular goitre is a simple goitre. As time progresses as a result of repeated involution and hyperplasia, multiple nodules develop gradually. These nodules increase in size and number with advancing years. The thyroid acini are divided into three types depending upon the stage.

Resting stage: The acini are lined by flattened cells, large and are filled with dense homogenous colloid.

Secretory Stage: the Acini are lined by cuboidal epithelium and colloid does not stain intensely.

Response Phase: Acini are lined with columnar cells and are filled with highly stained vacuolated colloid.

I. Stage of hyperplasia

It is due to increase in TSH, which is secreted as a response to low levels of circulating thyroid hormones.

Histology : Here the acini are hyperplastic and distorted by invagination of epithelium. The acini are lined with tall columnar cells and the colloid is less in quantity.

II. Colloid Phase

The acini are lined by cuboidal epithelial cells. The concentration of iodine is less than that of normal gland. When there is increase in supply of iodine, the thyroid gland undergoes spontaneous involution.

III. Nodular Phase

It is an irreversible phase of goitre and is due to the repeated stimulation of thyroid gland. The processes hypertrophy, hyperplasia and involution take place repeatedly. Faulty areas of involution which are associated with colloid distension will compress the normal glandular tissue. This along with newly formed fibrous tissue results in the nodule to become encapsulated.

Macroscopically, nodules may be single or multiple. The nodules may be pale yellow/pink and opaque in appearance. Dissolution of the follicles may lead to cyst formation.

Histology : Nodular goitre appears like a colloid goitre. It consists of poorly defined fibrous capsule surrounding colloid filled acini, which are lined by low cuboidal cells.

RETROSTERNAL GOITRE

Most retrosternal goitres develop from lower pole of nodular goitre. Very few retrosternal goitre develop from ectopic thyroid tissue. If there is a short neck and strong pretracheal muscles, negative intrathoracic pressure tends to

pull the nodules into superior mediastinum. A retrosternalgoitre is often symptomless. It usually receives its blood supply from the inferior thyroid vessels.

Retrosternal goitre may be

1.Substernal – commonest type. The lower border of thyroid lies behind the sternum.

2.Intrathoracic – No thyroid gland is seen in the neck. The Diagnosis is by radioiodine scan.

3.Plunging type – when intrathoracic pressure raises, the lower border lies in the neck.

A retrosternal goitre however can cause symptoms which may be life threatening.

• Dyspnoea

• Dysphagia

•Pressure on the great veins at thoracic inlet

•In severe cases there may be obstruction of the superior vena cava.

A retrosternalgoitre may be malignant or toxic. A chest radiograph in retrosternal goitre shows widening of the soft tissue shadow in superior

mediastinum sometimes along with calcification and often causing compression and deviation of trachea.

COMPLICATIONS OF MNG

1. Secondary Thyrotoxicosis

The toxicity in nodular goitre is due to the hyperactivity of the internodular thyroid tissue than due to the nodules. There are families of immunoglobulins which bind to the receptor sites of the thyroid stimulating hormone on the follicular cells of the membranes. These immunoglobulins have a prolonged action than TSH.

A few cases of MNG may have PLUMMER'S disease in which some of the nodules may be overactive as a result of autonomous function of the nodules.

2.Tracheal compression

It may be due to gross displacement of trachea. It commonly occurs due to haemorrhage into a nodule, retrosternal goitre and long standing multinodular goitre.

3.Malignant change

This is one of the most controversial subject which is still not yet settled. Malignant transformation is an uncommon complication. The incidence of carcinoma in MNG has been reported to be 5-10%. Sokal has reported that 4%

to 17% of multinodular goitres develop thyroid cancer. The malignancy occuring is usually of pappilary type.

APPROACH TO MULTINODULAR GOITRE

The thyroid nodules in multinodular goitre may be palpable or hidden and symptomatic or asymptomatic. Thyroid nodules less than 1-2 cms are usually not palpable. The gland may be abnormal or normal in structure and function.

Case history

The symptoms are the important evidence to know whether the patient is in hyper or hypo thyroid state. The patient or the family members may have noticed alteration in mental activity such as irritability or excitability. The patient may give history of alteration in temperature tolerance, perspiration and loss/gain in weight, altered bowel habits and appetite , visual disturbances or palpitation. Pressure symptoms like dyspnoea, dysphagia and hoarseness of voice may occur with multinodular goitre.

History regarding diet, ingestion of goitrogenic foods like cabbage, soyabeans and thyroid inhibiting drugs should be elicited. History of inhabitation in endemic area and family history of thyroid disorders should be recorded.

General examination

In general examination, the signs of hyper or hypothyroidism are to be noted. The extremities of the patient will be hot and moist in hyperthyroidism and cold and dry in cases with hypothyroidism. Tremors of hand and tongue should be noted. Eye signs characteristic of primary thyrotoxicosis are Stelwag's sign, Van Graef's sign, Moebius sign and Joffroy's sign.

Local examination

Inspection

Inspection is the most important part of examination. It provides lot of information. Swelling of the thyroid gland is confirmed by movement ondeglutition. To identify the retrosternal extension of the goitre, one must look for the lower border of the enlarged thyroid gland.

FIG 1 : CLINICICAL PICTURE OF MULTINODULAR GOITRE

FIG 2 : MULTINODULAR GOITRE IN MALE

Palpation

The thyroid gland is palpated both from behind and in front of the patient. During palpation size, shape, surface, skin over swelling, consistency and extent of the gland is noted.

The surface is bosselated with gross variation of consistency in MNG, where as in cases of thyroid carcinoma the consistency is hard, with indistinct irregular margin and irregular surface. If lower border of the gland is not felt at the suprasternal notch, it suggests retrosternal goitre. Examination of carotid pulsation, regional lymph nodes and position of trachea should be done routinely.

INVESTIGATIONS FOR MNG

I. Tests for thyroid function

1.Thyroid hormones (T4 and T3) assay

2. Pituitary thyroid axis (TSH) assay

3.Free thyroid hormone measurements (FT4 and FT3).

4. Tests of thyroid binding proteins

5. Hypothalamic – pituitary axis (TRH test)

II.Dynamic and Imaging studies of the Thyroid

1.Radioactive iodine uptake (RAIU) study

- T3 Supression test
- TSH stimulation test
- Perchlorate discharge test

2.Thyroidscintigraphy

3.Miscellaneous radioisotope imaging tests

- Gallium/ thallium
- Other radiopharmaceuticals – DMSA

III.Assessment of thyroid anatomy

- Ultrasound scan
- Computerised tomography (CT)
- Nuclear magnetic resonance imaging (NMRI).

IV.Tissue diagnosis

Fine Needle Aspiration Cytology (FNAC)

Core needle biopsy

V.Measurement of thyroid autoimmunity

- Anti-thyroglobulin antibodies
- Antimicrosomal antibodies

• Long acting thyroid stimulator (LATS)

• Thyroid stimulating immunoglobulins (TSI)

VI. Miscellaneous tests

• X-ray of the neck – AP and lateral vews

• X-ray of the chest - PA view

• Indirect laryngoscopy

• Thyroglobulin assay

• Calcitonin assay

ULTRASOUND SCAN

It represents the first modality of investigation that has made it possible to establish the physical state of thyroid lesion before surgery. The thyroid nodularity evaluation with normal or enlarged volume can be performed with a much higher sensitivity by high-resolution ultrasonography when compared with palpation. By ultrasonographic study, solid, cystic and mixed solid cystic nodules can be differentiated.

Among solid nodules, lesions of high or normal echogenicity can be distinguished from those with reduced echogenicity by comparison with normal thyroid gland and the neighboring muscular tissue. This helps in determining

the nodules to be investigated further by FNAC to exclude malignancy. It also has to be emphasized that the sonological appearance of a nodule per se does not exclude malignancy of the gland. Ultrasound also cannot be used to differentiate between functioning and nonfunctioning nodules.

FINE NEEDLE ASPIRATION CYTOLOGY (FNAC)

For the past 15-20 years, there has been a remarkable change in the approach to diagnosis and management of thyroid nodules. FNAC has become a test of utmost importance in the investigation and management of thyroid nodules. It involves the use of a smaller needle (Gauge 23-25) and 10-20 ml syringe. This technique provides material for cytological rather than a histological interpretation of the thyroid. The nodule is fixed between the fingers and thumb of one hand and the needle is injected into the lesion with the other hand. Suction is applied in the syringe to create a negative pressure. The needle is then moved back and forth in the nodule in different directions, by maintaining the negative pressure. A smear is prepared by using the material in the syringe. Fixed with 95% alcohol, stained and then studied..

There are four main categories in which the results fall, malignant, benign, suspicious and inadequate. In case of inadequate sample, the aspirate should be repeated. Papillary, medullary, anaplastic carcinoma and thyroiditis can be diagnosed using FNAC. Follicular adenoma cannot be differentiated form follicular carcinoma by FNAC, as presence of capsular and vascular invasion is important feature for the diagnosis of follicular carcinoma. When

FNAC is reported as follicular adenoma or suspicious of malignancy, surgery has to be performed to confirm the pathology.

RADIOIODINE UPTAKE AND THYROID SCAN

Cassen and his co-workers in 1951 were among the first to implement radioisotope scanning for diagnosis of diseases. They selected thyroid gland as the first organ for studying. The remarkable avidity of thyroid gland for radioiodine permitted visualization of the gland even with primitive scanning equipment available during that time.

Radioiodine uptake

Radioiodine is tested by administering a known amount of radioactive iodine to the patient and measuring the percentage accumulated in the thyroid gland by an external counting device. The radionuclide of choice is I 123. The radioiodine is given by mouth either in capsule or liquid from and the measurement is taken at a known time after ingestion.

The measurement depends on the function of the thyroid and the size of iodine pool or to be more precise the plasma inorganic iodine. Originally the test was used for the differentiation of normal people from hypothyroid and hyperthyroid patients. Which was later proved wrong.

Causes of increased radio iodine uptake

1.Hyperthyroidism

- •Graves disease
- • Toxic MNG
- • Toxic adenoma

2. Recovery form thyroiditis

3. Iodine deficiency

4. Dysharmonogenesis except trapping defect

5. After stopping anti-thyroid drugs

Causes of decreased radioiodine uptake

1. Iodine load

- • Dietary
- • Radiographic contrast agents
- • Medicines with inorganic iodine

2.Thyroxine or other thyroid medication – factitious thyroiditis

3. Ectopic thyroid

4. Hypothyroidism

5.Radio nuclide capsules not ingested or digested

6.After severe exercise

THYROID SCINTIGRAPHY

a.RoutineScintigraphy

Thyroid Scintigraphy became possible after the development of the rectilinear scanner by Casson. Now imaging in thyroid scinigraphy is performed by using by anger camera with a pinhole collimator. The radionuclide I123 is administered orally as a capsule and scintigrams are obtained 3-6 hours later. Recently Technetium 99m (99m TC) which is normally taken up by thyroid, like iodine, is widely used.

The scan has been used for:

1. Determining the size of the gland

2.Determining whether the nodule concentrates the radioiodine or (99mTC) or not.

3.Determining if retrosternal shadow on chest x - ray is due to thyroid.

4.Determining whether a lump in the tongue or track of thyroglossal duct containing functioning thyroid gland or ectopic thyroid.

5. For evaluation of toxic multi nodular goitre

b.Whole body Scintigraphy for thyroid metastases

Whole body Scintigraphy study is designed to provide information about the presence or absence of functioning metastases from a differentiated thyroid carcinoma. It should be done only after performing a total thyroidectomy because if it is done when there is a significant amount of normal thyroid tissue, the radio iodine localizes preferentially in the normal tissue and metastases are not made out.

Autoradiographic studies have shown that the metastatic thyroid carcinoma have about 1% of the uptake of normal thyroid gland. 1 or 2 mci of I131 is used. Whole body Scintigram should be performed about 4 weeks after surgery to allow endogenously secreted thyroid hormones to be metabolized and Thyroid stimulating harmone to raise. Blood is examined for TSH and thyroglobulin before I131 is administered. A whole body scintigraphy scan is obtained 48-72 hours after the radioiodine dose has been administered.

MISCELLANEOUS RADIOLOGICAL STUDIES

COMPUTERIZED TOMOGRAPHY (CT)

Computerized tomography has no place in routine evaluation of patients with thyroid disease. The following are the indications for CT.

1.Thyroid cancer with spinal metastases.

2. Substernalgoitre not concentrating iodine.

3.Recurrent cancer in neck not taking up iodine

HORMONAL ASSAY

Total thyroid hormones

Total T4 and T3 are measured using specific radioimmunoassay. Since they are highly protein bound, their values depends upon the levels of binding proteins present in serum. The normal total plasma T4 is approximately 8 micro g/dl and plasma total T3 is 0.15micro g/dl.

Causes of high level of thyroid hormones

Hyperthyroidism Increased binding proteins

Hereditary

Pregnancy

Active hepatitis

Oral contraceptive

Porphyria

New born

Antibody to thyroid hormones

Pituitary resistance to thyroid hormones

Acute medical illness

Causes of low levels of thyroid hormones

Hypothyroidism Decreased binding proteins

Hereditary

Androgens

Nephrotic syndrome

Glucocorticoids

Cirrhosis of liver

Low T3 and low T4 (sick euthyroid)

Low T3 syndrome

TESTS OF THYROXINE BINDING PROTEINS

Thyroxine binding capacity (TBC) is measured indirectly by quantitating the capacity of the binding sites in serum, those which are not carrying hormones. This is done using T3 RESIN UPTAKE TEST (T3RU) and normally

is in the range of 25% to 35%. If there are a lot of unoccupied binding sites over the proteins, the tracer will bind there and T3RU is low and vice versa.

Knowledge of T3, T4 and T3RU values are usefull in determining if the problem is due to thyroid diseases, or due to a binding protein abnormality. If both tests are abnormal towards the same direction, the thyroid is at fault. In contrast to it if one test is high and the other is low, the defect is due to the carrier proteins.

PITUITARY THYROID AXIS – TSH

Thyroid stimulating harmone radioimmunoassay became available in 1965. When T4 and T3 are normal and TSH is above normal, it is called as subclinical hypothyroidism. But older assay could only differentiate TSH levels of 1 Iu/ml or 2 Iu/ml and since many euthyroid individuals have TSH levels of 0.5 Iu/ml to 2.0 Iu/ml, assay could not differentiate suppressed values from normal values

With the introduction of immune radiometric assay (IRMA) and amplified enzyme linked immunoassay (AEIA) techniques, TSH levels even less than 0.3 micro units/ml can be detected. TSH is an extremely valuable aid in diagnosis, hypothyroid patients have high levels and hyperthyroid patients have low levels of TSH, provided pituitary insufficiency is excluded. When T3 and T4 normal and TSH in undetectable it is called subclinical hyperthyroidism.

HYPOTHALAMIC PITUITARY AXIS (TRH TEST)

TRH was isolated, characterized and synthesized in 1968. This is tested by injecting TRH intravenously and assessing the ability of pituitary gland to secrete TSH. A normal response is rise in TSH. The rise in TSH is maximal at 20-30 minutes with return to normal levels by 60-90 minutes. In cases of hyperthyroidism, the pituitary gland is suppressed by thyroid hormone and there is no rise in TSH even after injection of TRH. This test was of great value in early times for understanding the physiology and pathophysiology of hypothalamic pituitary thyroid interaction and it was clinically valuable in diagnosis of borderline hyperthyroidism.

PROPHYLAXIS - PLAN OF ACTION IN INDIA

The Government of India launched a NATIONAL GOITRE CONTROL PROGRAMME. The objectives of the programme are as follows:

1. Initial survey to identify magnitude of problem in the country

2. Production and supply of iodized salt to the endemic regions

3. Health Education & Publicity

4. To undertake monitoring of the quality of iodized salt assessing urinary iodine excretion pattern and monitoring of Iodine Deficiency disorder

5. Re-survey in goiter endemic regions after five years continuous supply of iodized salt to assess the impact of the control programme. The result of re-survey in some areas has revealed that the prevalence of goiter has not been controlled as desired.

TREATMENT OF MULTINODULAR GOITRE

Several treatment modalities are available for patients with Multi Nodular Goitres. The selection of best therapeutic option depends on several factors, including size of goitre, location, presence and severity of compressive symptoms, and the presence or absence of thyrotoxicosis.

THYROID-HORMONE-SUPPRESSIVE THERAPY

As Thyroid stimulating harmone is regarded as a growth factor for the thyroid epithelial cells,treatment with levothyroxine in doses enough to suppress TSH has been used for years to reduce or prevent growth of thyroid nodules. However, the effectiveness of this treatment has remained controversial. A clinical trial of 78 patients with non-toxic multi nodular goiter who were treated with levothyroxine or a placebo for a period of nine months and then were followed up for an additional nine months. Results showed a 58% reduction in volume of goitre assessed by ultrasonography versus a 4% reduction in placebo group, but this effect was lost after levothyroxine therapy was stopped. In a review of seven non randomized trials of suppressive harmone therapy for non-

toxic goiter, it was found that 60% of patient had decrease in goiter size during the period of thyroid hormone therapy. The decrease was found to occur within the first three months of treatment, and a better response was noted in those patients with diffusethyromegalyrather than nodular goiters.

The efficacy of levothyroxine therapy in preventing the recurrence of goiter growth after hemithyroidectomy is less clear. Several non randomized trials show that levothyroxine therapy is effective for these cases, but randomized controlled trials have failed to demonstrate a significant reduction in the recurrence of goiter. It has also been showed that in patients with multinodulargoitre, levothyroxine suppression therapy may prevent the formation of new nodules by interfering with the process of goitrogenesis, though it may not cause regression of all the clinically apparent nodules.

Due to known risks associated with subclinical hyperthyroidism as a result of levothyroxine suppression therapy, caution is essential when considering this management option in post-menopausal patients, particularly in those patients with evidence of low bone mass, the elderly patients, and those patients with cardiac disease, in those whom the risk of this therapy may be increased.

RADIOIODINE THERAPY

Radioiodine (RAI) has been effectively and widely used for the treatment of toxic multi nodular goiters. Administered usually as a single dose, orally it is rapidly concentrated in the thyroid tissue and results in the destruction of toxic

nodules of the thyroid in period of two to four months. Some patients, particularly in those with large goiters or severe hyperthyroidism, may need more than one dose to achieve euthyroidism. Radioiodine administered is preferentially accumulated in the hyper functioning nodules of thyroid and, so, subsequent rates of hypothyroidism are lower than in patients who are treated with radioiodine for Graves' disease.

Patients with severe thyrotoxicosis, particularly those with cardiac diseases and the elderly, may be pre-treated with antithyroid drugs (methimazole or propylthiouracil). There is evidence that propyl thiouracil, but not methimazole, may reduce the effectiveness of subsequent radioiodine therapy in these patients. Although RAI has not been traditionally considered as a treatment option for patients with non-toxic MNGs, several studies have shown that it is both safe and effective.

This treatment modality has the advantage of resulting in significant reduction in goitre size (30–60%), along with improvement in obstructive symptoms in most of the patients. In one study RAI was shown to be more effective than levothyroxine suppressive therapy in reducing goiter size. Transient hyperthyroidism may be seen in the first two weeks after treatment, and permanent hypothyroidism has also been reportedin up to 45% of patients.Pre-treatment with recombinant human thyroid stimulating harmone (rhTSH) has been evaluated in recent years as adjuvant to RAI in several studies as a method to enhance the efficacy of uptake of RAI in non-toxic thyroid tissue permitting the use of lower doses of RAI and enhancing reduction in goitre size.

Development of Graves' hyperthyroidism (with increased levels of TSH-receptor antibodies) has been described following treatment with RAI in patients with multinodular goitre and has been found to be more common in those patients with high thyroid peroxidase (TPO)antibody concentrations before the initiation of treatment.

SURGERY

Multinodular goitre is mostly an irreversible stage. So, surgery is the treatment of choice in young patients, for cosmetic reasons, possibility of malignant transformation, and suspicious malignancies. Patients presenting with large, obstructive and substernal non-toxic multinodular goitres or those with no regress in growth are best managed with surgery. Complications of surgery in cases of large and substernal goiters are more commonly seen than in patients who undergo thyroidectomy for cervical goiters. Complications include injury to the trachea, recurrent laryngeal nerves and the parathyroid glands. In a study which included 34000 patients who underwent thyroidectomy, 1153 (3.4%) had substernalgoitre showed that this last group of patients were older, men and more likely to have a comorbid condition. The surgeries usually performed for multinodulargoitre are subtotal and total thyroidectomy. Hemithyroidectomy may be performed in special circumstances where there are aremicronodules in a single lobe of the thyroid gland.

SURGERY FOR NONTOXIC MNG

Most patients of multinodulargoitre are asymptomatic and do not require surgery. Surgery may be indicated on cosmetic grounds. Retrosternal goitre with tracheal obstruction is an indication of operation, as is the presence of dominant area of enlargement among the other nodules, which may be neoplastic.

Choice of surgery:

a. Total thyroidectomy along with immediate and lifelong replacement of thyroxine.

b. Any form of partial resection in order to conserve sufficient functioning thyroid tissue to serve normal function and also eliminating the risk of hypothyroidism ,which accompanies total thyroidectomy. Partial resection aims at removing bulk of the gland and leaving upto 8 grams of relatively normal thyroid tissue i.e., subtotal thyroidectomy. More often the multinodularity is asymmetrically and distributed with one lobe more significantly involved than the other lobe, under these circumstances total lobectomy on the more affected side is the may be performed with either little or no intervention on the other less affected side.

In many cases, the causative factors persists and recurrence is likely to occur. Surgery for recurrent nodular goitre is difficult and hazardous. Due to this reason many surgeons prefer total thyroidectomy in young patients. After a

subtotal thyroidectomy it has been customary to give suppressive doses of thyroxinein order to suppress TSH secretion and thereby aiming at preventing recurrence.

SURGERY FOR TOXIC MNG

In toxic MNG the principle behind surgery is by reducing the mass of overactive tissue. Cure is probable if the remnant thyroid tissue can be surgically reduced below a critical mass. This may result in a reduction in the level TSAbs or it may be that the circulating TSAbs however high its level may be can only produce limited hypertrophy and hyperplasia when the thyroid tissue mass is meager. In a case of toxic MNG with autonomous toxic nodules, surgery cures by removing all the overactive nodules. Thereby allows suppressed normal thyroid tissue to function again.

The extent of resection of thyroid tissue depends on the gland size, patient’s age, experience of the operating surgeon, the need to minimize recurrent toxicity and the wish to avoid postoperative thyroid replacement therapy. Young patients who have a small gland are at greater risk of recurrence even when there is a very small remnant thyroid tissue.

In recent times, there is an increasing trend towards total thyroidectomy, as it simplifies the subsequent management and a permanent euthyroid state can be rapidly achieved on thyroid replacement therapy. In contrast to this a patient with large goitre who wishes to avoid postoperative medication may be suitable

for subtotal thyroidectomy where 4-5 gms of thyroid tissue is left behind in each lobe.

In toxic Multinodular goitre, surgery is the treatment of choice. Treatment with radioiodine is highly unreliable in toxic MNG because blood flow through such goitres is not homogenous or symmetrical as in diffuse goitre. As a result uptake of radioiodine by the goitre is irregular and many areas escape effective radiation from radioiodine and hyperthyroidism continues. For these reason surgery is the treatment of choice for patients with hyperthyroidism due to Multinodular goitre.

SUBTOTAL THYROIDECTOMY

The patient is made to lie supine on the operating table, with the table tilted 15 degree at the head end in order to reduce venous engorgement. A sand bag is placed under the shoulders and the neck is extended to make the thyroid gland more prominent. General anaesthesia is administered through a flexible endotracheal tube preferably and good muscle relaxation obtained. A low color skin crease incision is made two finger breadth above the suprasternal notch. Upper and lower flaps of skin, subcutaneous tissue and platysma are raised upto the thyroid notch above and to the suprasternal notch below. The deep cervical fascia is incised in the midline. The strap muscles are split and not divided as a routine but may be divided if great exposure is required. In 30% of patients, middle thyroid veins is present which is short and lies transversely passing directly into the internal Jugular veins. It require ligation and division. The main

blood supply to the gland is the superior thyroid artery, which must be ligated and divided with caution and in a secure manner. The superior thyroid artery is divided close to the gland to prevent the injury to external laryngeal nerve. The lobe is then freed so it can be rotated out of its bed. The inferior thyroid artery away from the gland. The recurrent laryngeal nerve should be identified along its course and injury should be prevented. The parathyroid glands are protected by identification before resection and avoiding ligatures and sutures close to hilum of the identified gland. If one of the parathyroid gland is inadvertently excised or devascularised, it should be autotransplanted within the sternomastoid muscle in several fragments. Subtotal resection of each lobe is carried out, leaving behind a remnant of between 3 and 5 grams on each side. Complete haemostasis is obtained by ligation of individual vessels and by suturing of thyroid remnants to the tracheal fascia. The pretracheal muscles and cervical fascia are sutured and the wound is closed with or without suction drainage to the deep cervical space.

TOTAL THYROIDECTOMY

The technique of operation is same as in subtotal thyroidectomy, except that no remnant thyroid tissue is left over in total thyroidectomy. Identifying and sparing recurrent laryngeal nerves and parathyroid glands is very important as these structures are more prone to injury.

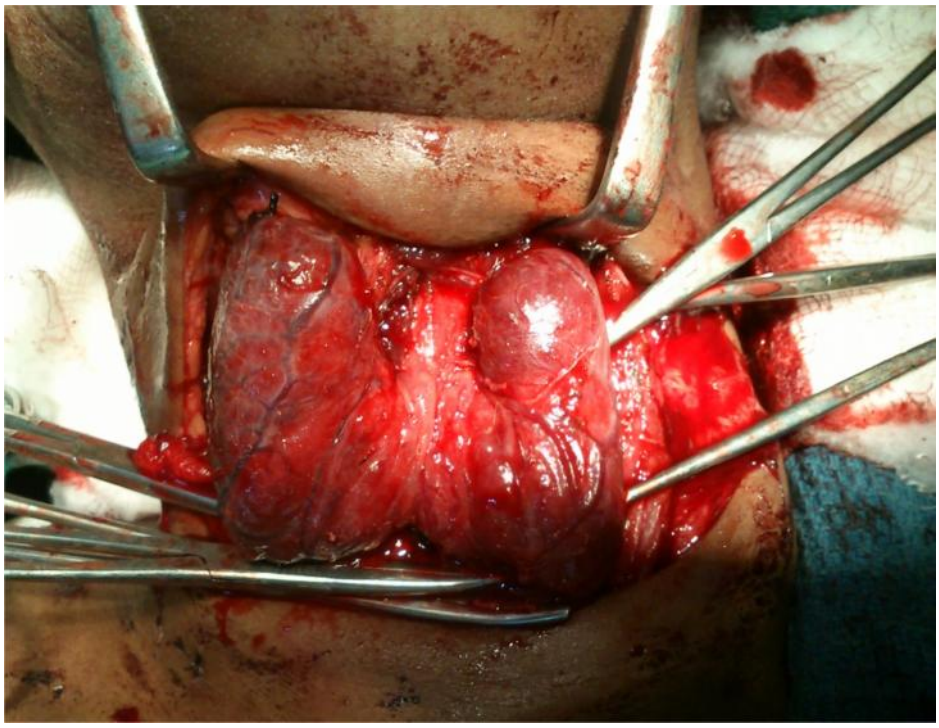


FIG 3 : EXPOSURE OF BOTH THE LOBES OF THYROID

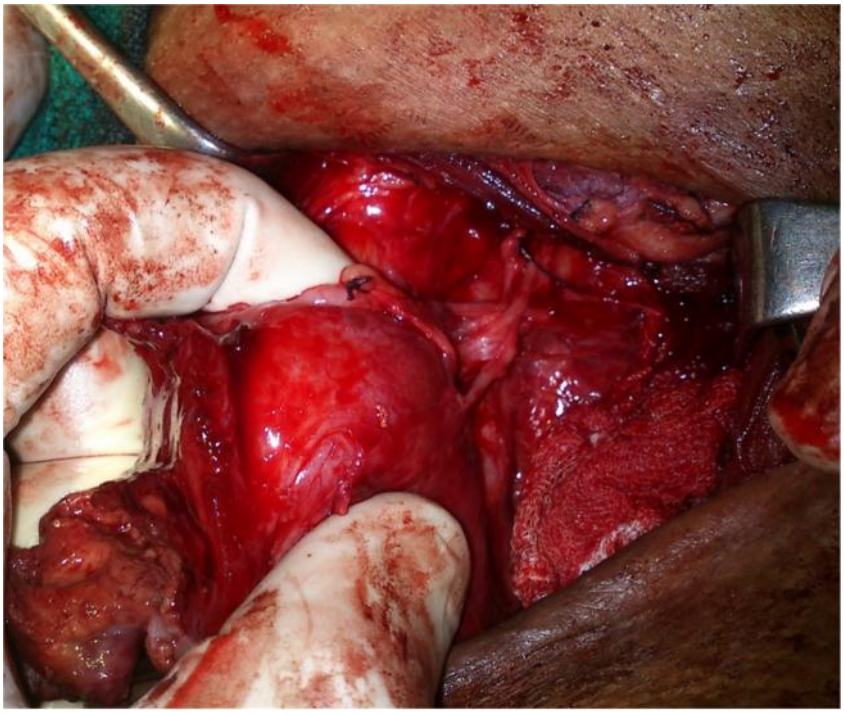


FIG 4 : LIGATION OF THE SUPERIOR THYROID PEDICLE

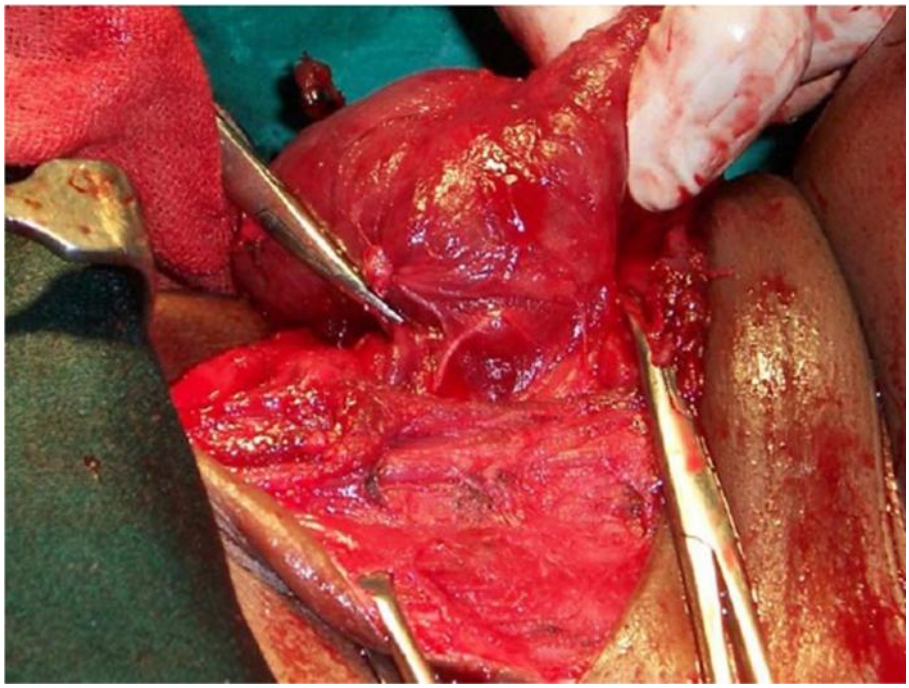


FIG 5 : IDENTIFICATION OF RECURRENT LARYNGEAL NERVE

FIG 6 : SPECIMEN OF MULTINODULAR GOITRE

POSTOPERATIVE COMPLICATIONS

HAEMATOMA

A tension haematoma deep to thedeep cervical fascia is usually due to slipping of ligature of the superior thyroid artery; occasionally haemorrhage from a remnant of thyroid gland or a thyroid vein may be responsible. immediate surgical exploration is necessary if the patient develops respiratory distress. On rare occasions, it may be necessary to open the sutures in the bedside to relieve tension before shifting the patient to the theatre to evacuate the haematoma and to arrest the site of bleed.

RESPIRATORY OBSTRUCTION

Respiratory distress in most cases is due to laryngeal oedema and very rarely due to kinking or collapse of trachea. The most important cause of laryngeal oedema is due to a tension haematoma. Trauma to the larynx by anaesthetic and surgical manipulation is a main contributory factor particularly if the goitre is very vascular.

Unilateral or bilateral recurrent nerve paralysis will not usually cause immediate postoperative respiratory obstruction. Unless laryngeal oedema is also present but the former two will aggravate the obstruction. If release of the tension haematoma does not relieve airway obstruction immediate tracheal intubation must be carried out. Elective endotracheal ventilation may be carried

out for several days, until the oedema subsides; steroids are given to reduce the oedema. Tracheostomy is rarely necessary.

POSTOPERATIVE THYROID CRISIS

Thyroid crisis is an acute exacerbation of hyperthyroidism. It occurs patient who is in thyrotoxicosis has been inadequately prepared for surgery. Very rarely throtoxic crisis may occur following an unrelated operation in a thyrotoxic patient. It is characterized by tachycardia, high fever, delirium and restlessness, progressing towards cardiac failure. Symptomatic and supportive treatment is administered for dehydration, hyperpyrexia and restlessness. This is carried out in the form of administration of intravenous fluids, administration of oxygen, cooling the patient with ice packs, diuretics for cardiac failure, digoxin for uncontrolled atrial fibrillation, intravenous hydrocortisone and sedation.

Specific treatment is by lugol's iodine 10 drops 8 hourly by mouth, carbimazole 10-20 mg 6 hourly or sodium iodide 1 gm intravenously. Propronalol 40 mg 6 hourly orally will block the adverse beta adrenergic effects. This should be given by careful intravenous administration under precise electrocardiographic control.

PARATHYROID INSUFFICIENCY

This results due to removal of parathyroid glands or interference with their blood supply as a result of trauma to parathyroid end artery. The incidence is less than 0.5% and most cases dramatically present 2-5 days after surgery. Very rarely the onset is delayed for 2-3 weeks. Early symptoms are peri oral numbness and tingling sensation. It is commonly transient in nature and quickly controlled by oral administration of calcium. If severe carpo pedal spasm occurs, 20 ml of 20% solution of calcium gluconate is given intravenously and is later supplemented with oral calcium.

RECURRENT LARYNGEAL NERVE PARALYSIS

Recurrent laryngeal nerve injury may be unilateral or bilateral; transient or permanent. Transient paralysis occurs in about 3% of the nerves and usually recovers in about 3 weeks to 3 months. Permanent paralysis is a extremely rare condition if the nerves have been identified during surgery. If there is no recovery within this period, organic injury to the nerve should be suspected. This may be as a result of stretching, bruising of the nerve or inclusion in a ligature, it is seldom divided. The prognosis regarding recovery is poor if the nerve is divided. Repair of the divided nerve may be attempted, but the results are not always productive.

In a study conducted in France, encompassing 192 thyroidectomies during 50 months with a follow up of 8 months gave the following results regarding the complications:

Death – 0.08%

Haematoma-1.6%

Chyle leak – 0.2%

Abscess –0.5%

Temporary and permanent hypoparathyroidism – 20% and 4% respectively. Temporary and permanent recurrent laryngeal nerve palsy – 2.9% and 0.5% respectively.

Chung Yau Lo et al performed a study on 500 thyroidectomies in Hong Kong. They observed that the incidence of temporary and permanent recurrent laryngeal nerve palsy as 5.2% and 1.4% respectively.

HYPOTHYROIDISM

This usually occurs during the first 2 years but may be delayed for more than 5 years. Hypothyroidism is often insidious and difficult to diagnose. The incidence is higher than used to be thought and figures of 20 to 45% have been reported after operations on toxic nodular goitres with internodular hyperplasia. It represents a change in the autoimmune response form stimulation to destruction of thyroid cells. The treatment consists of administration lifelong

supplementation of thyroxin to prevent myxedema after estimating thyroid profile post operatively at 1 week and 1 month.

RECURRENT THYROTOXICOSIS

This is either due to subsequent hyperplasia of the tissue that has been left or inadequate removal of thyroid tissue. It is common in primary toxic goitre but very rare in secondary thyrotoxicosis. Further surgery should be avoided if possible. The best results are obtained by radioiodine therapy or by administering anti-thyroid drugs.

OTHER COMPLICATIONS

Wound infection

Hypertrophic or Keloid Scar

Stitch granuloma

MATERIALS AND METHODOLOGY

The material of the present study consists of patients admitted with nodular thyroid swelling at the surgical units of Tirunelveli Medical College Hospital, Tirunelveli. Total of 50 patients who were admitted in our hospital from December 2013 to September 2014 were included in the study.

After admission, a detailed history and thorough clinical examination was carried out which was entered in the proforma. The patients were investigated. The investigations included complete blood analysis, urine analysis, thyroid function tests, blood sugar and urea estimation,serum creatinine, blood grouping and typing, x-ray of the neck antero posterior and lateral views and chest X-ray, ultrasound neck and ENT examination. All patients had a thyroid profile and FNAC done. Few selected patients underwent computerized tomography scan before surgery. These patients underwent surgery and all the excised thyroid specimen were sent for Histopathological examination. Patients were discharged after removing the sutures and were asked to come for follow up. Post operative thyroid profile was done on 1st post operative week and at 1 month. They were advised to take the needful medications accordingly. Only those patients with clinical evidence of multinodular goiter were taken up for the study randomly, excluding malignancies detected preoperatively and the results were compared with other studies.

RESULTS

TABLE 1:AGE DISTRIBUTION OF MULTINODULAR GOITRE

AGE IN YEARS	NO OF CASES	PERCENTAGE
20 – 30	10	20%
30 – 40	16	32%
40 – 50	11	22%
50 – 60	08	16%
ABOVE 60	05	10%

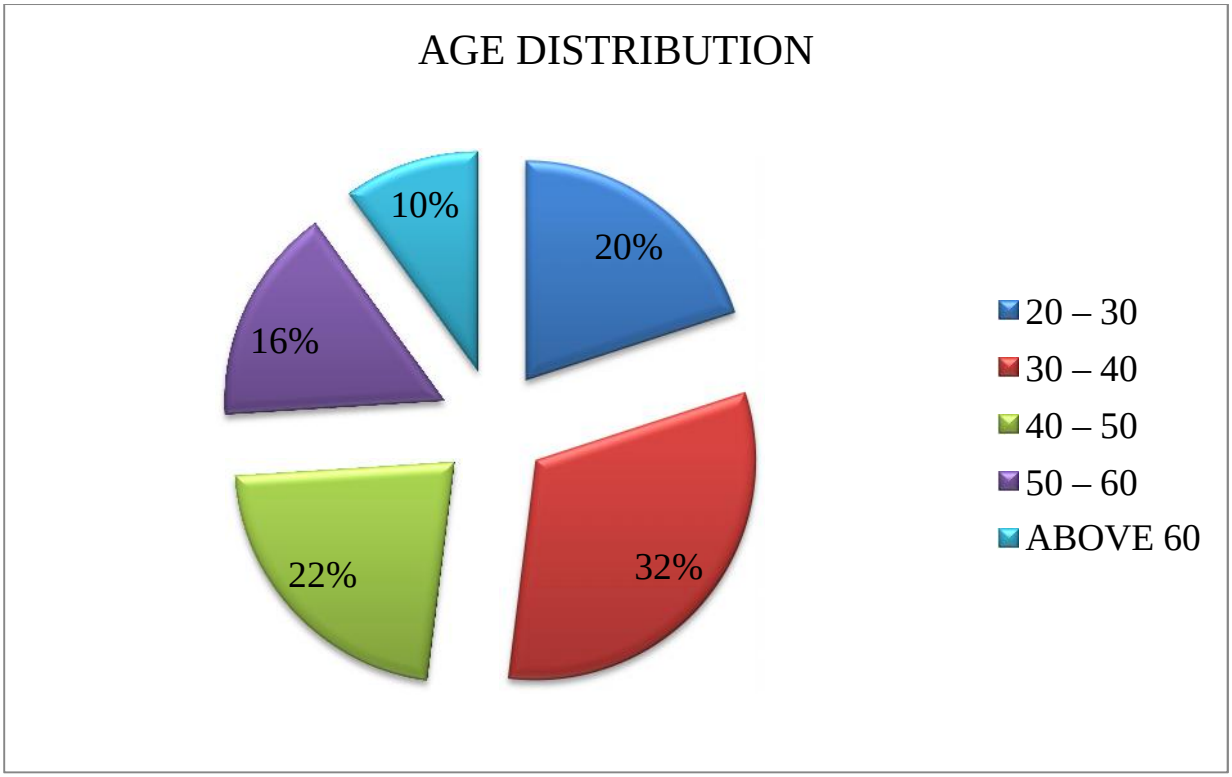


TABLE 2: SEX DISTRIBUTION OF MULTINODULAR GOITRE

SEX	NO OF CASES	PERCENTAGE
MALE	3	6%
FEMALE	47	94%

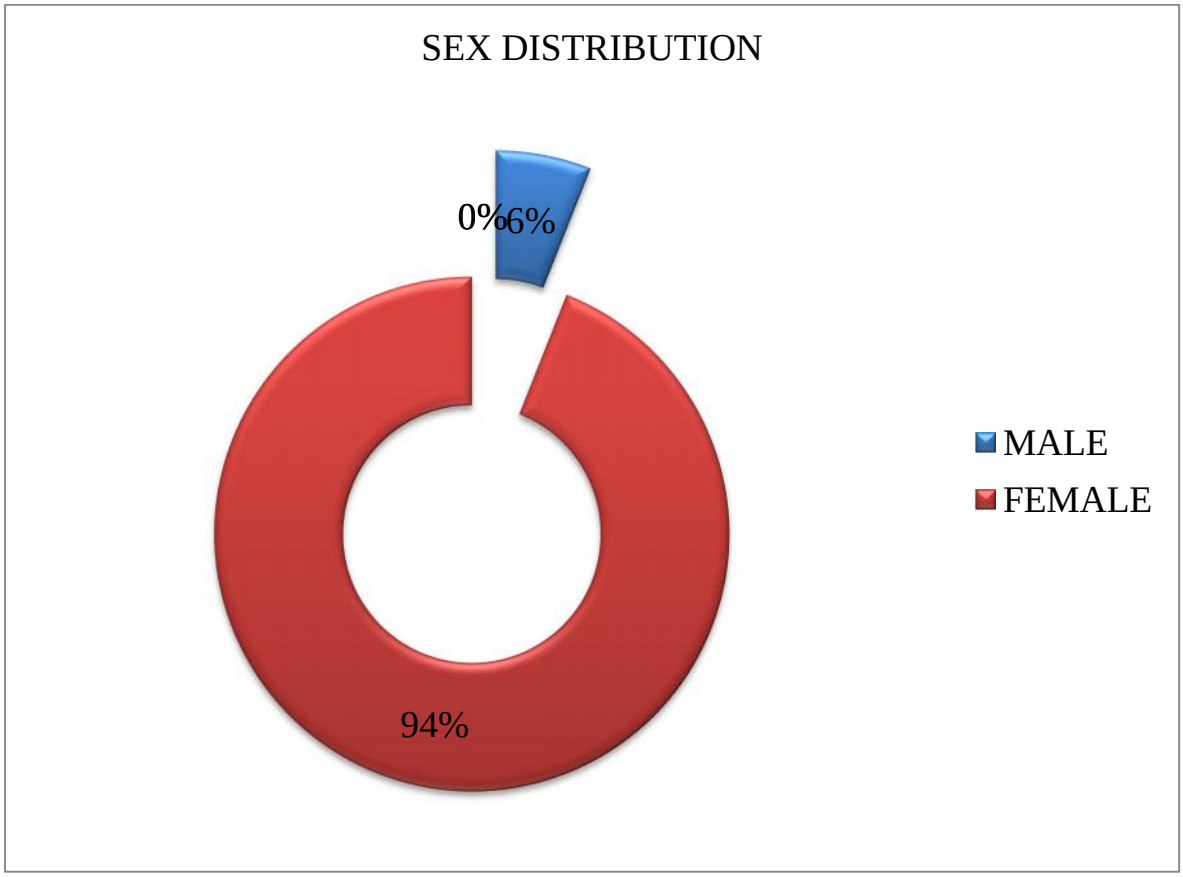
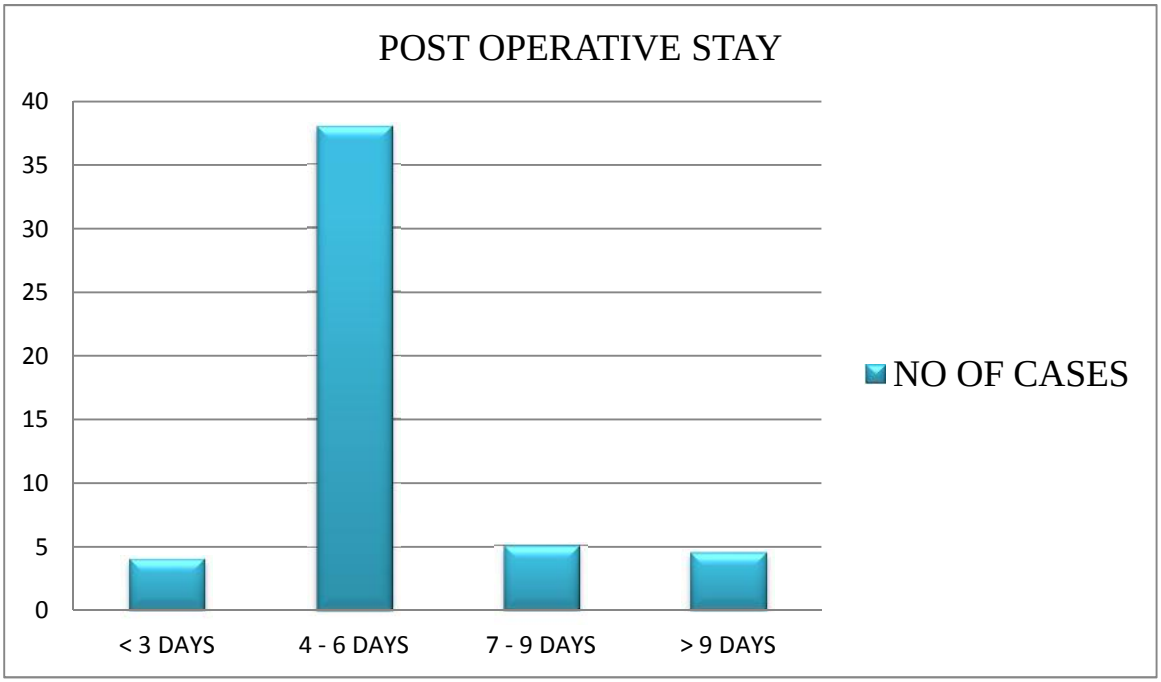


TABLE 3: DAYS OF POST OPERATIVE STAY FOLLOWING THYROID SURGERIES

NO OF DAYS OF POST OPERATIVE STAY	NO OF CASES	PERCENTAGE
LESS THAN 3 DAYS	04	8%
4 – 6 DAYS	38	76%
7 – 9 DAYS	05	10%
MORE THAN 9 DAYS	03	6%



AVERAGE POST OP STAY – 5.3 DAYS

TABLE 4: INCIDENCE OF PRESENTING COMPLAINTS IN MULTINODULAR GOITRE

PRESENTING COMPLAINTS	NO OF CASES	PERCENTAGE
SWELLING	50	100%
PAIN	24	48%
HEAT / COLD INTOLERANCE	06	12%
INCREASED / DECREASED APPETITE	03	06%
DYSPNOEA	09	18%
TREMORS	08	16%
INSOMNIA	05	10%
PALPITATION	16	32%
DYSPHAGIA	22	44%
HOARSENESS OF VOIVE	10	20%

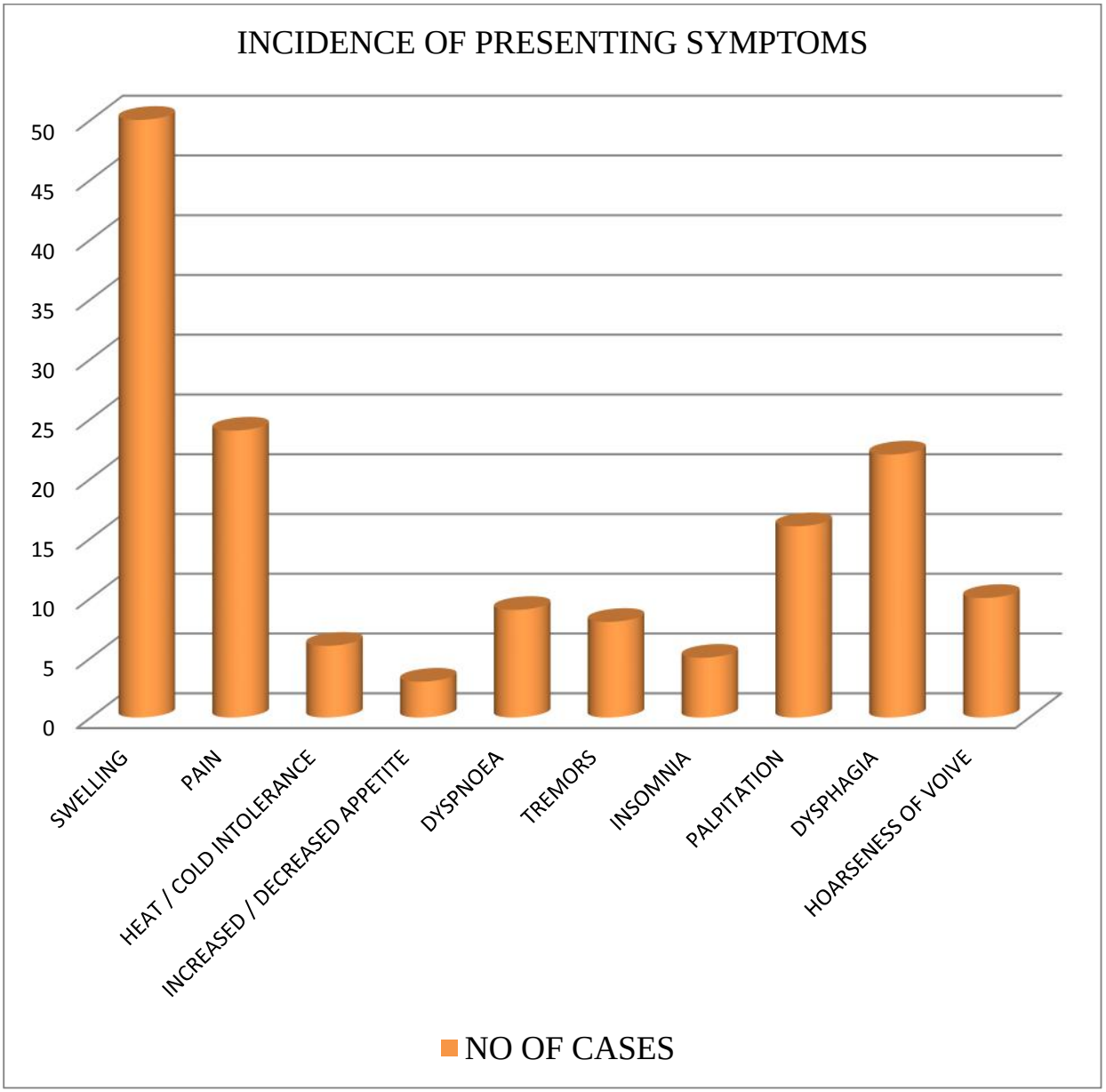

INCIDENCE OF PRESENTING SYMPTOMS
50
45
40
35
30
25
20
15
10
5
0
SWELLING
PAIN
HEAT / COLD INTOLERANCE
INCREASED / DECREASED APPETITE
DYSPNOEA
TREMORS
INSOMNIA
PALPITATION
DYSPHAGIA
HOARSENESS OF VOIVE
NO OF CASES

TABLE 5: THYROID STATUS ON PRESENTATION

THYROID STATUS	NO OF CASES	PERCENTAGE
HYPOTHYROID	0	0%
EUTHYROID	43	86%
HYPERTHYROID	7	14%

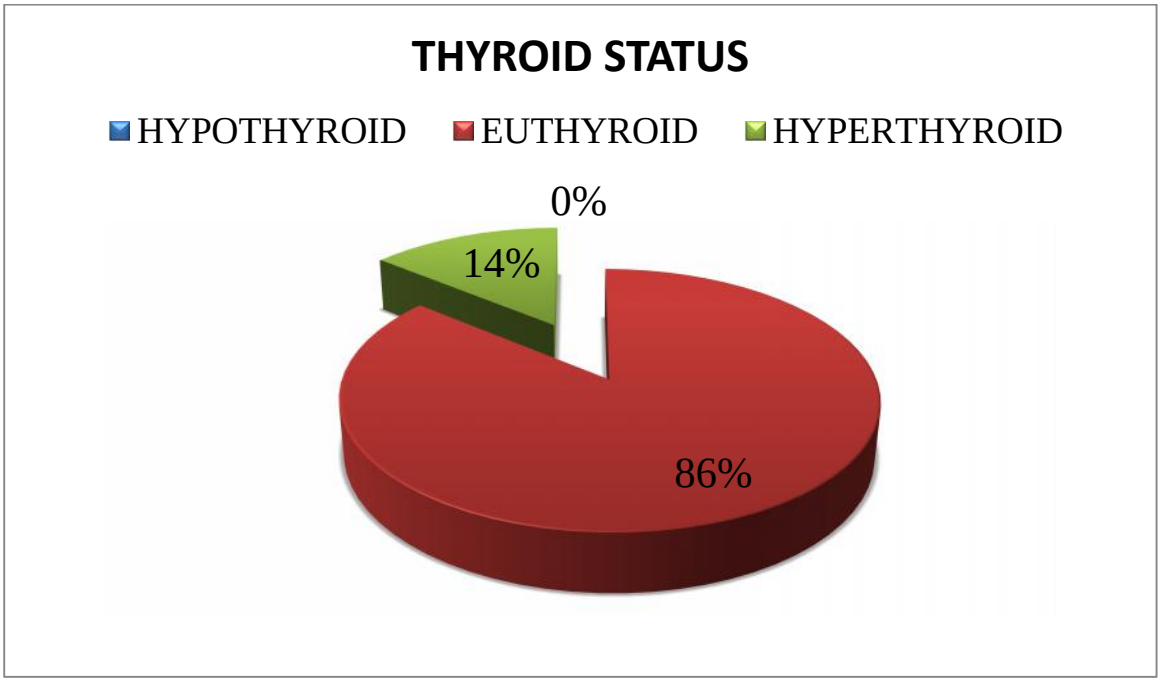


TABLE 6: FINE NEEDLE ASPIRATION CYTOLOGY IN MULTINODULAR GOITRE

FNAC REPORT	NO OF CASES	PERCENTAGE
COLLOID NODULAR GOITRE	32	64%
HASHIMOTO'S THYROIDITIS	11	22%
ADENOMATOUS GOITRE	4	8%
FOLLICULAR NEOPLASM	2	4%
INCONCLUSIVE	1	2%

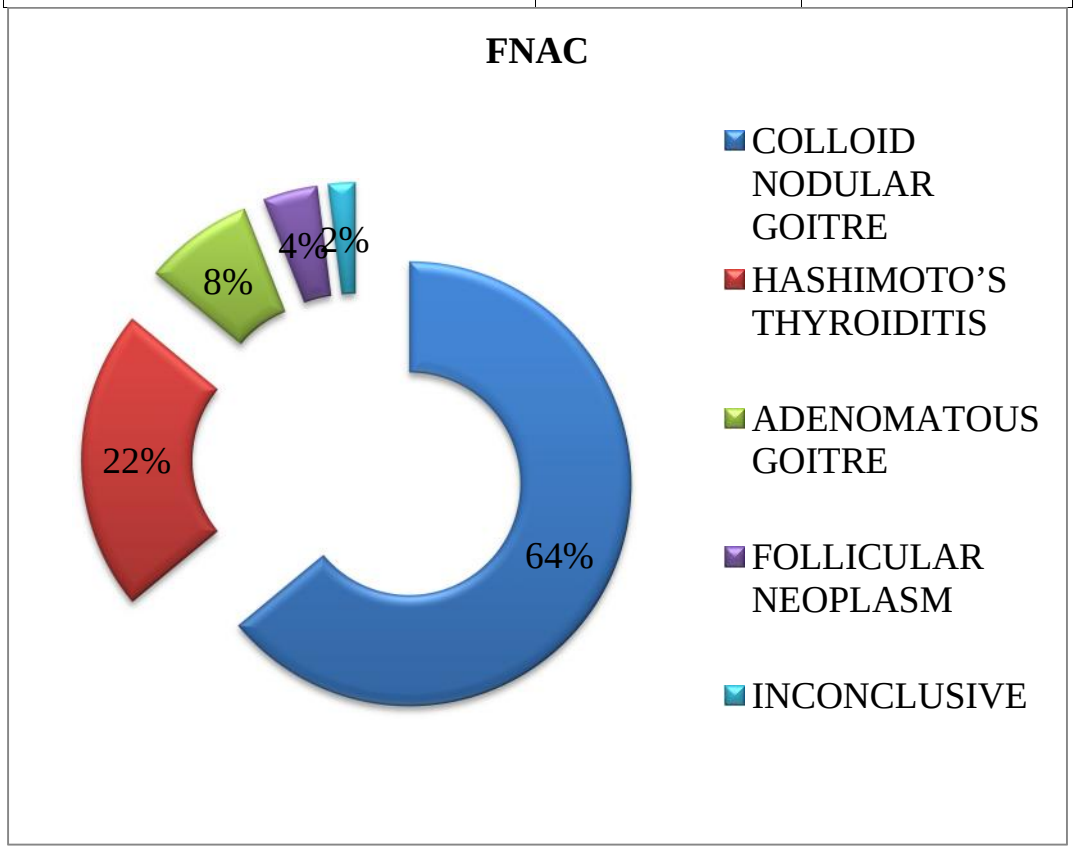


TABLE 7 : SURGERIES PERFORMED

NAME OF SURGERY	NO OF CASES	PERCENTAGE
LOBECTOMY	1	2%
SUBTOTAL THYROIDECTOMY	5	10%
TOTAL THYROIDECTOMY	44	88%

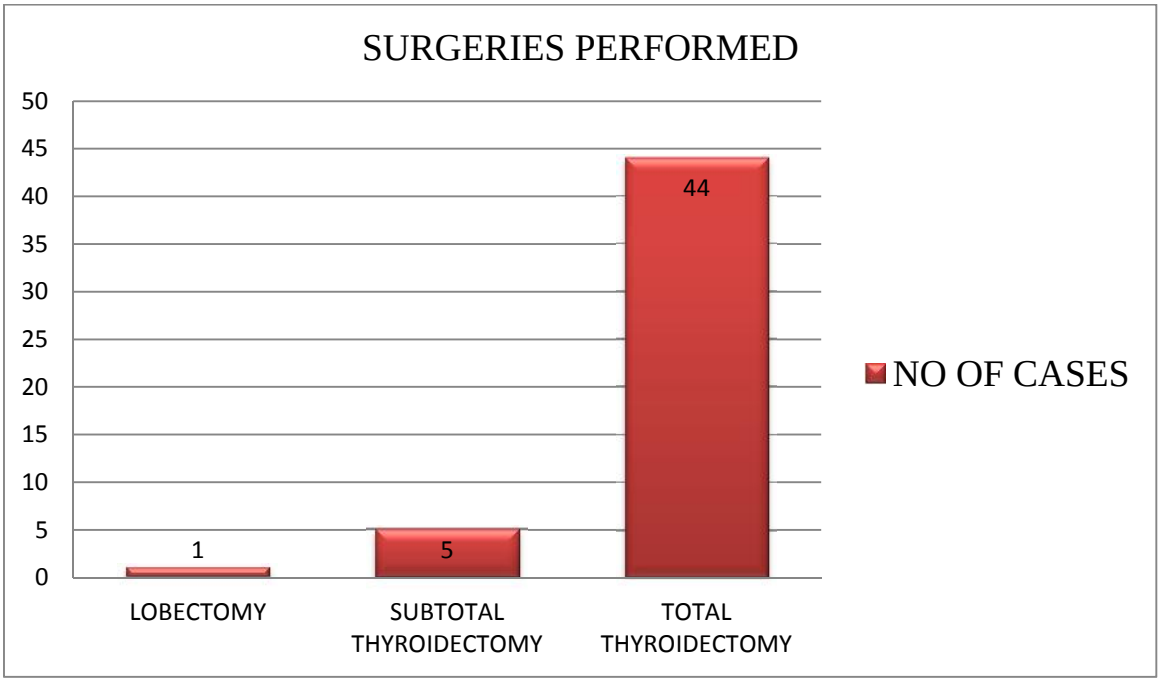


TABLE 8: INCIDENCE OF POST OPERATIVE COMPLICATIONS

COMPLICATION	NO OF CASES	PERCENTAGE
RECURRENT LARYNGEAL NERVE INJURY	2	4%
HYPOPARATHYROIDISM	1	2%
CERVICAL HEMATOMA	0	0%
SUPERIOR LARYNGEAL NERVE INJURY	0	0%
INFECTION	0	0%

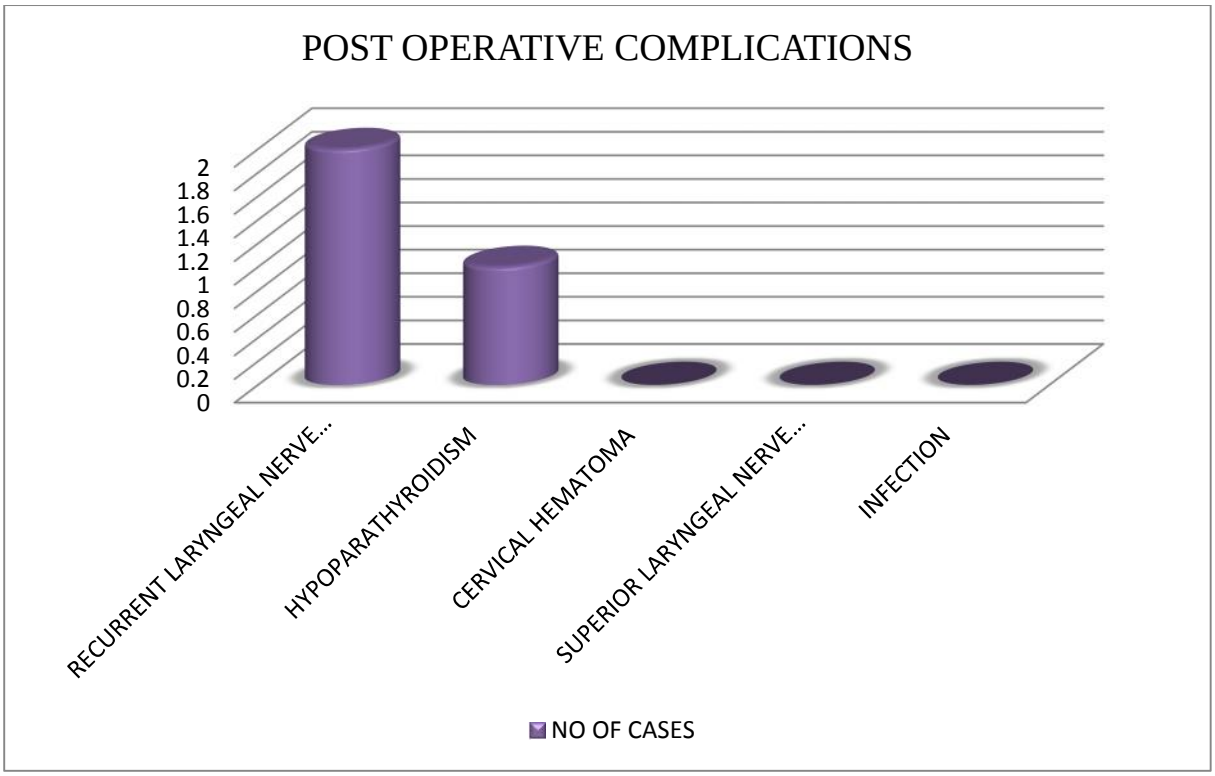
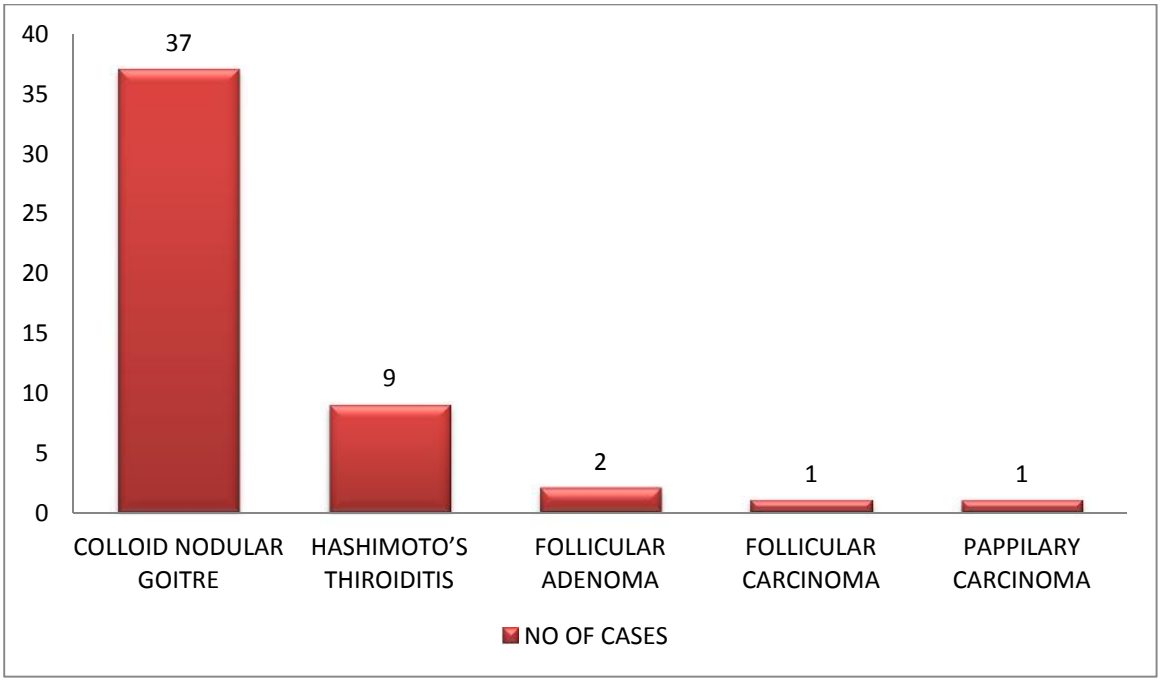


TABLE 9 : HPE REPORTS IN MULTI NODULAR GOITRE

HPE REPORT	NO OF CASES	PERCENTAGE
COLLOID NODULAR GOITRE	37	74%
HASHIMOTO'S THIROIDITIS	09	18%
FOLLICULAR ADENOMA	02	4%
FOLLICULAR CARCINOMA	01	2%
PAPPILARY CARCINOMA	01	2%



DISCUSSION

In this study, fifty patients diagnosed as Multi nodular goitre without any evidence of malignancy were evaluated in terms of history taking and clinical examination. Relevant investigations were performed and surgery was performed after FNAC. The histopathological examinations of the specimen were done post operatively. The results were compiled, analyzed and are depicted in tables1 to 9.

In our study, among the 50 cases three were male which constitutes 6% of the study group. The remaining 47 cases were females (94%). Antanio Rios – Zumbudio et al conducted a study in 2004 which showed 89% of cases in the study group were female.

Majority of the cases were in the 30 – 40 years age group (32%), followed by the age group of 40 – 50. This compared to the analysis of 1280 cases of Multinodulargoitre performed by Bremer and Moll Night which showed maximum incidence between 40 and 50 years, shows that a lesser age group is commonly involved in our population and the Mean age of incidence was 42.26.

The average post operative stay among the 50 cases studied was 5.3 days. 76% of the cases were discharged between 4 to 6 days of post operative stay.

The presenting complaint was a swelling in all the cases studied (100%). The swelling was associated with pain in 48% of the cases. Pressure symptoms

like dysphagia, dyspnoea and hoarseness of voice were present in 44%, 18% and 20% of cases respectively with an average of 27.3% which is comparable to the study by Rios Zumbudio et al who had a result of 28.5% of cases presenting with pressure symptoms.

Of the 50 cases of Multinodular goiters studied, 7 cases were hyperthyroid on presentation which constitutes 14% of the cases. This is low compared to the 22% hyperthyroidism cases among the 301 multinodulargoitre cases studied by Rios – Zumbudio et al. this may be due to the early age at presentation of the cases in our study, compared to the age of presentation in the western population.

All the cases were taken up for surgery, 88% of cases underwent total thyroidectomy and 10% of cases underwent subtotal thyroidectomy. One case with multinodularity of one lobe of the thyroid - largest measuring 0.7 cm underwent right lobectomy, who was followed up for 3 months and the opposite lobe was found to be normal.

The Fine Needle Aspiration Cytology reports of the 50 cases showed Nodular Colloid Goitre (64%) as the most common FNAC finding followed by Hashimoto’s Thyroiditis (11%). The FNAC report was follicular neoplasm for 2 cases, so total thyroidectomy was performed in those cases to rule out malignancy.

Post operative complication occurred in three cases. In two cases who underwent surgery developed recurrent laryngeal nerve injury was present of whom one patient developed stridor and tracheostomy was performed. The other patient recovered following management with elective ventilation and steroid therapy. One patient developed post operative hypoparathyroidism. She was treated with calcium supplementation. Post operative complications such as superior laryngeal nerve injury, cervical hematoma and infection were not present in any of the cases.

The post operative histopathological examination of the resected specimen showed that 37% of the cases were Colloid nodular goitre and 18% of cases had features suggestive of Hashimoto's thyroidits. 1 case operated for FNAC report of follicular neoplasm turned out to be follicular carcinoma (Hurthle cell variant) on examination of the specimen. 1 case with inconclusive result on FNAC was reported as papillary carcinoma on histopathological examination of the specimen. Incidence of malignancy in multinodular goitre accounts for 4% which is comparable to the studies by Gondolfi et al who had a result of 6.7% in a retrospective study of 81 cases.

CONCLUSION

- MULTINODULAR GOITRE is more common among females and in the age group of 30 to 40 years and is more common among females.
- The chief complaint in most of the patients is swelling in front of the neck and is associated with pain in 48% of the cases.
- The average post operative stay in the hospital was 5.3 days. Post operative stay in hospital has to be reduced. Thyroidectomy can be done as a day care or short stay procedure in our hospital as is the recent trend in developed countries. However, the applicability of these practices to thyroid surgery remains controversial. Day care surgery can be promoted in selected and educated patients as this will be the future of thyroid surgeries
- Hyperthyroidism in multinodular goitre was present in 14% of cases. Hyperthyroidism occurs in cases of multinodular goitre in the natural evolution of the disease and the patient must be treated and brought to euthyroid state before surgery.
- FINE NEEDLE ASPIRATION CYTOLOGY is a very useful investigation in the evaluation of Multinodular goitre except for that it cannot differentiate follicular adenoma from follicular carcinoma. Most of the cases had colloid nodular goitre in

multinolar goitre. Carcinoma in not uncommon in cases of Multinodular goitre. So, suspicion should always be present.

- Total thyroidectomy is the preferred surgery for multinodular goitre. But subtotal thyroidectomy may also be performed in cases in whom surgery is done for cosmetic reasons as in Hashimoto's thyroiditis. Hemithyroidectomy can be an option in Multinodular goitre if the nodules are confined to one lobe and the patient is aware of the possibility of recurrence and is willing for regular follow up.
- Post operative complications after thyroidectomies for multinodulargoitre are less in our institution as compared to various studies. Visualization of the recurrent laryngeal nerve during surgery is an important factor contribution to the low incidence of nerve injuries in our study group.

BIBLIOGRAPHY

1. Franceschi S. Epidemiologia del carcinoma della tiroide. In:Miani P eds. Il carcinoma della tiroide. Pisa: Pacini Editore,1992; 13-29.
2. Miani P, Piemonte M, Bacchi G, Miani C. Fattori prognosticie risultati terapeutici nel carcinoma della tiroide. In: Miani P eds. Il carcinoma della tiroide. Pisa: Pacini Editore,1992; 167-97.
3. Cole WH. Incidence of carcinoma of the thyroid in nodulargoiter. *Semin Surg Oncol* 1991; 7 (2): 61-3.
4. Koh KB, Chang KW. Carcinoma in multinodular goitre. *BrJ Surg* 1992; 79 (3): 266-7.
5. Mathai V, Idikula J, Fenn S, Nair A. Do long-standing nodular goitres result in malignancies? *Aust N Z J Surg* 1994;64: 180-2.
6. McCall A, Jarosz H, Lawrence AM, Paloyan E. The incidence of thyroid carcinoma in solitary cold nodules and in multinodular goiters. *Surgery* 1986; 100 (6): 1128-32.
7. Pelizzo MR, Toniato A, Piotto A, Bernante P. Cancer in multinodular goiter. *Ann Ital Chir* 1996; 67 (3): 351-6.
8. Sachmechi I, Miller E, Varatharajah R, et al. Thyroid carcinoma in single cold nodules and in cold nodules of multinodular goiters. *Endocr Pract* 2000; 6 (1): 110-2.
9. Hossein G. Changing concepts in the diagnosis and management of the thyroid nodules. *Endocrinology and Metabolism Clinics of North America* 1997; 26 (4): 777-800.

10. Franceschi S, Talamini R, Frassina A, Bidoli E. Diet and epithelial cancer of the thyroid gland. *Tumori* 1990; 76: 331-8.
11. Francis SG. The problem of nodular goitre. *Med Clin N Am* 1991; 75: 195-209.
12. Clark OH, Quan-Yang D. Thyroid cancer. *Med Clin N Am* 1991; 75: 211-34.
13. Miller, J.M. & Block, M.A. Functional autonomy in multinodular goiter. JAMA 1970, 214: 535-539.
14. Sokal, J.E. A long-term follow-up of nontoxic nodular goiter.Arch Int Med 1957, 99: 60-69.
15. Vander, J.B., Gaston, E.A. & Dawber, Th.R. The significance of nontoxic thyroid nodules. Ann Int Med 1968, 69: 537-540.
16. Plummer, H.S. The clinical and pathological relationship of simple and exophthalmic goiter. Am J Med Sci 1913, 146:790- 795.
17. Cole, W.H., Slaughter, D.P. & Rossiter, L.J. Potential dangers of nontoxic nodular goiter. JAMA 1945, 127:883-888.
18. Blum, M., Shenkman, L. & Hollander, C.S. The autonomous nodule of the thyroid: correlation of patient age, nodule size and functional status. Am J Med Sci 1975, 269: 43-50.
19. Hamburger, J.I. Solitary autonomously functioning thyroid lesions. Am J Med 1975, 58: 740-748.

20. Hamburger, J.I. Evolution of toxicity in solitary nontoxic autonomously functioning thyroid nodules. J Clin Endocrinol Metab 1980, 50: 1089-1093.

21. Belfiore, A., Sava, L., Runello, F., Tomaselli, L. & Vigneri, R.Solitary autonomously functioning thyroid nodules and iodine deficiency. J Clin Endocrinol Metab 1983, 56:283-287.

22. Lerro, S., Losa, M., Trisorio, M.T. & Liuzzi, A. Free thyroid hormone levels and TSH response to TRH in patients with autonomous thyroid adenomata and normal T3 and T4. Clin Endocrinol 1985, 23: 373-378.

23. Elte, J.W.F., Haak, A., Frolich, M., Wiards, K.S. & van Wermeskerken, R.K.A. Autonomously functioning euthyroid multinodular goitre. Neth J Med 1977, 20: 1-4.

24. Smeulers, J., Docter, R., Visser, T.J. & Hennememann, G.Response to thyrotrophin-releasing hormone and triiodothyronine suppressibility in euthyroid multinodular goitre.Clin Endocrinol 1977, 7: 389-397.

25. Emrich, D. & Bahre, M. Autonomy in euthyroid goitre:maladaption to iodine deficiency. Clin Endocrinol 1978, 8:257-265.

26. Hamburger, J.I. & Hamburger, S.W. Diagnosis and managemen of large toxic multinodular goiters. J Nucl Med 1985,26: 888-892.

27. Parker, J.L.W., Ratcliffe, J.G. & Alexander, W.D. Sporadic non-toxic goitre. Acta Endocrinol 1977, 85: 497-507.

28. Wiener, J.D. & de Vries, A.A.A. On the natural history of Plummer's disease. Clin Nucl Med 1979, 3: 180-190.

29. Wiener, J.D. Long-term follow-up in untreated Plummer's disease (autonomous goiter). Clin Nucl Med 1987, 12:198-203.

30. Smeulers, J., Docter, R., Visser, T.J. & Hennemann, G. Acute thyrotoxicosis in multinodular goitre. Neth J Med 1977, 20:275-277.

31. Smeulers, J., Visser, T.J., Docter, R. & Hennemann, G.Occasional thyroxine and triiodothyronine hypersecretion in euthyroid multinodular goitre. Neth J Med 1980, 23:152-154.

32. Hamburger, J.I. & Taylor, C.I. Transient thyrotoxicosis associated with acute hemorrhagic infarction of autonomously functioning thyroid nodules. Ann Int Med 1979, 91: 406-409.

33. McCall, A., Jarosz, H., Lawrence, A.M. & Paloyan, E. The incidence of thyroid carcinoma in solitary cold nodules and in multinodular goiters. Surgery 1986, 100: 1128-1132.

34. Wiener, J.D. & Frensdorf, E.L. Thyroid autonomy (Plummer's Disease) with contralateral malignancy-mere coincidence? Acta Med Scand 1976, 200: 509-512.

35. Bondeson, L. & Ljungberg, O. Occult thyroid carcinoma at autopsy in Malmo, Sweden. Cancer 1981, 47: 319-323.

36. Gemsenjager, E., Heitz, Ph.U., Staub, J.J. & Girard, J.Thyrotropin secretion in carcinoma of the thyroid. Surg Gynecol Obstet 1980, 151: 205-208.

37. Frey, W.K. Die Aufgaben der konventionellen Rontgendiagnostik der Schilddriise. Akt Endokr Stoffw 1983,4: 2-8.

38. Studer, H., Peter, H.J. & Gerber, H. Toxic nodular goitre. Clin Endocrinol Metab 1985, 14: 351-372.

39. Seth, J., Kellett, H.A., Caldwell, G. et al. A sensitive immunoradiometric assay for serum thyroid stimulating hormone: a replacement for the thyrotrophin releasing hormone test? Br Med J 1984, 289: 1334-1336.

40. Kerr, D.J. & Alexander, W.D. Is the TRH test usually unnecessary. Lancet 1984, ii: 1161- 1162 (letter).

41. Carayon, P., Martino, E., Bartalena, L. et al. Clinical usefulness and limitations ofserum thyrotropin measurement by 'ultrasensitive' methods. Hormone Res 1987, 26: 105- 117.

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ANNEXURE I - PROFORMA

Name : Age/Sex:

Address :

IP.NO :

D.O.A : D.O.S : D.O.D :

COMPLAINTS:

H/O PRESENTING ILLNESS

H/O Swelling

H/O Pain

H/O Increased / decreased appetite

H/O Weight loss/gain

H/O Excessive sweating

H/O Heat / cold intolerance

H/O Excitability, irritability, H/O restlessness

H/O Insomnia

H/O Tremors

H/O Palpitation

H/O Muscle weakness

H/O Visual disturbance

H/O Diplopia

H/O Protrusion of eyes

H/O Chest pain

H/O Dyspnoea

H/O Dysphagia

H/O Hoarseness of voice

Menstrual history:

Treatment history:

Drug intake

Irradiation

Surgeries

GENERAL EXAMINATION

Built

Nutrition

Anaemia

Dyspnoea

Jaundice

Cyanosis

Generalised lymphadenopathy

Tremors

Leg edema / periorbital myxedema

Eye signs:

Pulse rate

Blood pressure

CVS

RS

ABDOMEN

CNS

LOCAL EXAMINATION OF NECK:

INSPECTION

Swelling :

- Site
- Size
- Shape
- Surface
- Skin over the swelling
- Surrounding area
- Number
- Movement on deglutition
- Movement on protrusion of tongue
- Position of trachea

PALPATION

- Warmth
- Tenderness

Site, size & shape

Surface

Consistency

Extent

Skin over the swelling

Mobility

Position of trachea

Kocher’s test

Pemberton’s sign

PERCUSSION

AUSCULTATION

INVESTIGATIONS :

Thyroid function tests:

T3

T4

TSH

ECG

X-ray:

Chest pa view

Neck AP and lateral

USG thyroid

FNAC

TREATMENT

Medical :

Surgery:

POST OPERATIVE COMPLICATIONS

Type of complication

Treatment given

HPE REPORT

FOLLOW UP:

Sl. No.	Name	Age	Sex	IP No.	Date of surgery	Post-op Stay	Swelling	Pain	Heat /Cold Intoslerance	Appetite (Increased or	Dyspena	Tremors	Insomnia	Palpitations	Dysphagia	Hoarseness of voice	Thyroid status
1	Vellathai	39	F	212	22/1	5	+	-	-	-	-	-	-	+	+	-	Hyper
2	Mariyakulanthai	55	F	4647	26/1	4	+	+	-	-	-	-	-	+	-	-	E
3	Kulalamani	45	F	4891	5/2	4	+	+	-	-	-	-	-	+	+	+	Hyper
4	Shanthi	22	F	4977	5/3	6	+	+	-	-	+	-	-	-	+	-	E
5	Poomari	33	F	15892	19/3	6	+	+	-	-	-	-	-	-	-	-	E
6	Mariammal	36	F	16410	21/3	5	+	+	-	-	+	-	-	-	+	-	E
7	Krishnaveni	31	F	14038	23/3	5	+	+	-	-	-	-	-	+	-	-	E
8	Karpagam	46	F	15445	9/4	4	+	-	-	D	-	+	+	+	-	-	Hyper
9	Muthulakshmi	40	F	20482	25/4	10	+	-	H	-	-	-	-	+	-	-	E
10	Kuttipappa	31	F	23310	26/4	5	+	-	-	-	-	-	-	-	-	-	E
11	Ansel Beevi	55	F	21450	26/4	6	+	-	-	-	-	-	-	-	-	-	E
12	Subbulakshmi	65	F	22462	27/4	4	+	-	-	-	-	-	-	-	+	+	E
13	Vellaiammal	60	F	21681	27/4	4	+	-	-	-	-	-	-	-	+	+	E
14	Mookkammal	35	F	23310	27/4	7	+	-	H	-	-	+	+	+	-	-	E
15	Seetha Lakshmi	51	F	27941	10/5	6	+	-	-	-	+	-	-	-	+	-	E
16	Lakshmi	32	F	43146	29/10	4	+	-	-	-	-	-	-	-	-	-	E
17	Seetha Lakshmi	71	F	26406	17/5	3	+	+	-	-	+	-	-	-	+	-	
18	Ayyammal	36	F	29816	18/5	4	+	-	-	D	-	+	+	+	-	-	E
19	Lakshmi	39	F	29636	20/5	4	+	+	-	-	-	-	-	-	+	-	E
20	Sarina	28	F	30342	21/5	6	+	-	-	-	-	-	-	-	-	-	E
21	Saraswathy	43	F	30330	30/5	5	+	-	-	-	-	-	-	-	+	-	E
22	Kavitha	36	F	31126	31/5	5	+	+	-	-	-	-	-	-	-	-	E
23	Raja	39	M	21707	1/6	5	+	-	-	-	+	-	-	+	-	-	E
24	Muthulakshmi	23	F	31441	1/6	3	+	+	-	-	-	-	-	-	-	-	E
S. No.	Name	Age	Sex	IP No.	Date of surgery	Post-op Stay	Swelling	Pain	Heat /Cold Intoslerance	Appetite (I or D)	Dyspena	Tremors	Insomnia	Palpitations	Dysphagia	Hoarseness of voice	Thyroid status
25	Ponnammal	37	F	32730	3/6	5	+	-	-	-	-	-	-	-	-	-	E
26	Ramalakshmi	33	F	32740	3/6	5	+	-	-	-	+	-	-	-	-	-	E
27	Geetha	52	F	34706	7/6	5	+	+	-	-	-	+	-	-	+	-	E
28	Balammal	65	F	38569	5/7	6	+	+									E
29	Kalaiselvi	28	F	40371	6/7	8	+		H								E
30	Shanthi	44	F	40979	8/7	3	+	+							+		E
31	Ramalakshmi	60	F	40345	9/7	4	+	+	-	-	-	-	+	-	-	-	E

32	Mohaideen Meeral	30	F	40329	13/7	4	+	-	-	-	-	-	-	-	+	+	E
33	Darwin	29	M	41618	16/7	9	+	+	H	-	+	+	-	+	+	-	Hyper
34	Muthukrishnan	60	M	47198	20/7	5	+	+			+				+	+	E
35	Shanmugathai	35	F	40330	23/7	6	+	-	-	-	+	+	-	+	-	-	Hyper
36	Sundari	50	F	42947	23/7	4	+	+	-	-	-	-	-	+	+	+	E
37	Mallika	24	F	43147	27/7	7	+	+	-	-	+	-	-	-	-	-	E
38	Rajammal	65	F	48407	19/8	7	+	-	-	-	-	-	-	-	+	+	E
39	Chinnammal	40	F	49810	19/8	3	+	+	-	-	-	-	-	-	-	-	Hyper
40	Chellathai	47	F	51363	31/8	5	+	-	-	-	+	-	-	-	+	-	E
41	Vasanthi	30	F	51391	3/9	4	+	+	-	-	-	-	-	-	-	-	E
42	Gowsalyadevi	22	F	53135	19/9	6	+	-	-	-	-	-	-	-	-	-	E
43	Indra	52	F	55279	21/9	4	+	-	-	-	-	-	-	-	-	-	E
44	Shenbagam	65	F	53951	25/9	6	+	+	-	-	-	-	-	-	+	+	E
45	Pathirakali	45	F	55328	27/9	6	+	+	-	-	-	-	-	-	-	-	E
46	Mary Testy Mona	28	F	53946	28/9	7	+	-	H	D	-	+	-	+	-	-	Hyper
47	Packialakshmi	49	F	58972	8/10	6	+	+	-	-	-	-	-	+	-	-	E
48	Sivanammal	32	F	58465	10/10	6	+	-	-	-	-	-	+	+	-	+	E
49	Amaravathy	50	F	58367	29/10	5	+	+	-	-	-	-	-	-	+	+	E
50	Jeya	45	F	59113	29/10	13	+	+	-	-	-	-	-	-	+	+	E

Master chart – Abbreviations

H - Heat Intolerance

C - Cold Intolerance

I - Increase In Appetite

D - Decrease In Appetite

E - Euthyroid

Hyper - Hyperthyroid

CNG - Colloid Nodular Goitre

AG - Adenomatous Goitre

HT - Hashimoto’s Thyroiditis

FN - Follicular Neoplasm

IC - Inconclusive

FA - follicular adenoma